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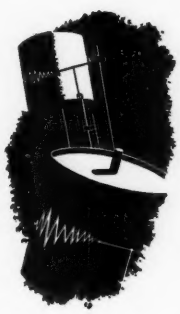

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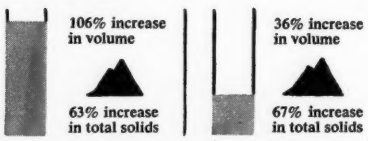

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Volume 247 JULY 17, 1952 Number 3

AUSCULTATION IN THE DIAGNOSIS OF COMPRESSION OF THE SUBCLAVIAN ARTERY*

EDWARD A. EDWARDS, M.D.,† AND HAROLD D. LEVINE, M.D.‡

BOSTON

COMPRESSION of the subclavian artery is well known as an essential aspect of the pathology of cervical rib, the scalenus syndrome and anomalies of the first thoracic rib. The demonstration of this compression, with or without resort to the so-called scalenus maneuver introduced by Adson and Coffey,[1] should be considered a routine prerequisite for the diagnosis of symptomatic cervical rib or the scalenus syndrome.[2] In this maneuver the arterial compression is usually appreciated through palpation of the radial artery at the wrist. By this means complete obliteration of the pulse is of course readily detectable, but partial obstructions are less easily recognized. We have found, however, that auscultation of the distal segment of the subclavian artery offers a more delicate means than palpation of detecting incomplete obstruction, the presence of a systolic murmur being used as the diagnostic sign.

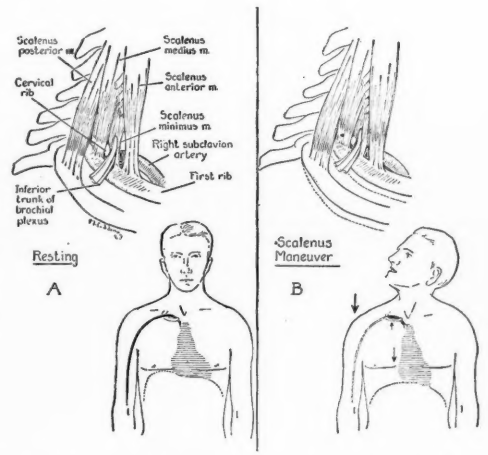

FIGURE 1. *Mechanism of Compression of the Subclavian Artery.*

In the subject represented, a cervical rib, heavy scalenus minimus muscle and wide scalenus anterior muscle are all present, yet the artery is unobstructed in the resting position. During the performance of the scalenus maneuver, the artery is squeezed by the tensed scalene muscles. It is further stretched over the elevated first rib as its proximal part follows the inspiratory descent of the heart and diaphragm, and its distal part descends with the manual depression of the shoulder.

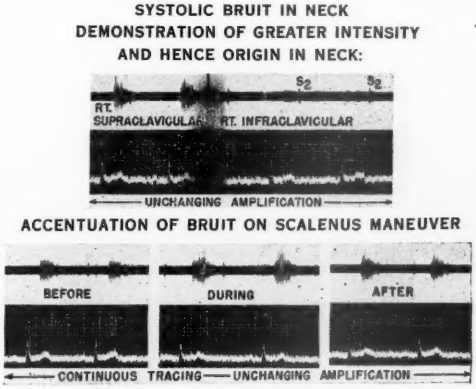

FIGURE 2. *Marked Systolic Murmur Heard over the Subclavian Artery in a Patient with Scalenus-Minimus Compression and Its Accentuation by the Scalenus Maneuver.*

The electrocardiogram is shown to indicate pulse phase of the murmur. S_2 is the second heart sound. Several irregularly spaced vibrations in the sound tracing are caused by extraneous noise.

METHOD

Steps in the scalenus maneuver may be stated briefly. The head is tilted sharply backward and to the side opposite the arm being tested. The chin is raised to face the affected side. The shoulder is sharply depressed by the examiner's hand. The patient takes a deep breath and holds it. Figure 1 indicates how the maneuver results in compression of the subclavian artery.

The stethoscope is applied to the artery in the subclavian fossa lateral to the sternomastoid and scalene muscles. In registering the murmur heard over the artery a microphone is substituted for the

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Aided by a grant from the Plymouth County Chapter of the Massachusetts Heart Association.

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stethoscope, its electrical output being fed into one channel of a multiple-channel electrocardiograph. The simultaneous electrocardiogram allows a determination of the pulse phase of the murmur.

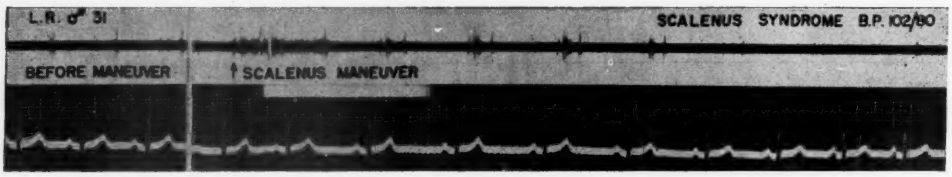

FIGURE 3. *Auscultation over the Subclavian Artery in a Patient with the Scalenus Syndrome.*
At rest the two heart sounds are noted. Performing the maneuver introduces stenotic-flow vibrations over several beats, but subsequently almost all sounds disappear as the obstruction becomes more complete.

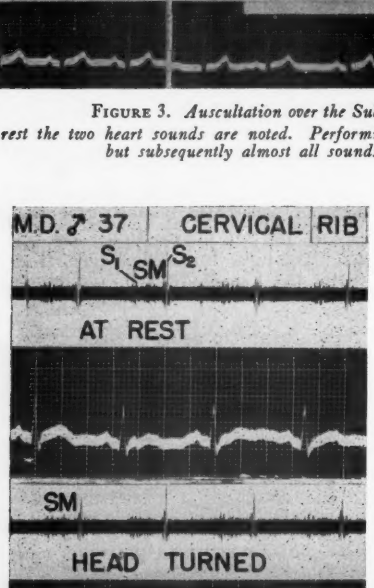

FIGURE 4. *The Systolic Murmur Heard with Cervical Rib and Its Progressive Accentuation by the Steps of the Scalenus Maneuver.*
S_1 and S_2 are the heart sounds, SM the systolic murmur. In the lowest tracing a muscle roar distorts the base line of the sound. S_1 is here blended with the stenotic-flow vibrations of the murmur.

A murmur due to subclavian-artery compression may be heard or registered in one of three circumstances:

The murmur may be heard with the patient at rest, indicating a constant partial obstruction of the vessel. In this instance the murmur is usually intensified by the scalenus maneuver (Fig. 2). The presence of sounds or of murmurs transmitted from the heart must be discounted, and one must similarly learn to disregard the roar caused by tensing of the muscles.

The murmur may be heard only after performing the maneuver, indicating temporary partial compression of the artery (Fig. 3 and 4).

No murmur may at first be heard on carrying out the maneuver. This may of course indicate the absence of arterial compression, but it may also be due to complete rather than partial arterial occlusion. Palpation of the radial artery while the maneuver is performed will differentiate complete and partial occlusion, and very gently repeating the maneuver should allow a murmur to be heard.

Differential Diagnosis

The systolic murmur may be considered diagnostic of subclavian-artery compression if one rules out a transmitted cardiac murmur or intrinsic disease of the artery. Arteriosclerosis often produces such murmurs but without variations induced by the scalenus maneuver. In one case of scalenus-minimus compression, a constant systolic murmur noted preoperatively (Fig. 2) failed to disappear after freeing of the artery, but it was no longer influenced by the scalenus maneuver. This was interpreted as evidence of atheroma at the site of compression, a lesion recently emphasized by Adson.[2] Aneurysm of the subclavian artery, spontaneous or secondary to a cervical rib, must also be excluded.

Mechanism of Murmur Formation

The murmur is comparable to that existing distal to the pneumatic cuff in sphygmomanometry.[3] Auscultation is found to be more sensitive than palpation in perceiving the pressure changes in

both circumstances. The systolic murmur heard distal to arterial obstructions is composed of three components: a few early systolic vibrations (impact) caused by the thrust of the systolic limb of the pulse wave; a more prolonged vibration starting slightly later but still in early systole (stenotic flow) due to flow through the narrowed segment of artery; and a few protodiastolic vibrations (recoil). The latter constitute sound transmitted in the blood stream by the closure of the aortic valve.[3] It is impossible to distinguish the impact and recoil vibrations from the first and second heart sounds when the latter are audible in the subclavian fossa (Fig. 4). The systolic murmur associated with arterial occlusion is probably maximal with an obstruction of medium grade (about 60 to 70 per cent).[4] The intensity and duration of the murmur are increased by the presence of a high pulse pressure, the three components of the murmur usually merging.

Conclusions

The finding of a systolic murmur by auscultation over the subclavian artery is a sensitive method of detecting proximal partial compression of that artery by anomalies of the cervical and first thoracic ribs or in the scalene syndrome. The murmur may be constant or may be brought out only by the scalenus maneuver. Transmitted cardiac murmurs and murmurs caused by intrinsic disease such as arteriosclerosis or aneurysm must be ruled out.

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THE ROUTINE USE OF QUINIDINE IN ACUTE MYOCARDIAL INFARCTION*

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PROVIDENCE, RHODE ISLAND

During the course of a study on the use of Dicumarol in acute myocardial infarction, the value of the routine use of quinidine in this condition was also investigated. In particular, the investigation was directed toward ascertaining whether or not the incidence of arrhythmias and sudden unexpected death could be altered. The first 55 patients in the Dicumarol study had received no quinidine and were therefore designated as a control group. The remaining 66 patients received 0.2 gm. of quinidine sulfate by mouth four times a day, at 8 a.m., 12 noon, 4 p.m. and 8 p.m. This dosage schedule was adopted as being convenient for nursing personnel and not interfering with patients' sleep. It did entail a rather long period without medication, but since it has been shown[1] that approximately 25 per cent of the maximum plasma level of quinidine after a given dose is still present twelve hours later, it was decided that this program might reasonably be given a trial. Then, in a group of 40 patients, alternate subjects were given 0.4 gm. of quinidine every eight hours, at 6 a.m., 2 p.m. and 10 p.m., in this way providing even distribution of the drug throughout the day and night without interfering with sleep. In a final group of 50 patients, alternate subjects received 0.6 gm. of quinidine at the same eight-hour intervals.

In this study only patients with a definite and typical history of chest pain occurring within seven days prior to admission were included. Moreover, clear electrocardiographic evidence of recent myocardial infarction was required. Patients dying within twenty-four hours of hospital admission were excluded. Actually, this restriction eliminated only a few patients who were moribund on admission. Five patients surviving more than twenty-four hours were excluded because they were too ill to take any oral medication. Each patient was seen daily, with particular attention being directed to the presence or absence of arrhythmias and toxic symptoms in those receiving quinidine. Electrocardiograms were taken about every ten days and more often when indicated. Patients were followed for six weeks, or until death or discharge.

The treated and control groups for each of the three dosage schedules were compared with reference to age, sex, previous myocardial infarction, estimated severity of the present infarction and the use of Dicumarol. The severity of the myocardial infarction was graded on a + to ++++ basis. Criteria used in estimating severity included the degree and duration of chest pain, the extent and persistence of blood-pressure drop, the presence of gallop rhythm and clear evidence of heart failure, the height and duration of the febrile response, the degree of elevation of the white-cell count and the magnitude of the electrocardiographic abnormalities. According to all these methods of comparison, the group receiving 0.4 gm. of quinidine and that receiv-

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ing 0.6 gm. corresponded closely with the control cases. The larger group of patients receiving 0.2 gm. of quinidine corresponded closely with its control group as regards estimated severity of infarction and the use of Dicumarol. However, as regards age, sex and the incidence of previous infarction, the treated and control groups at this dosage schedule were not strictly comparable. Only 41 per cent of the treated patients were sixty years of age or over, whereas 58 per cent of the control group fell in this category. Moreover, only 14 per cent of the quinidine group had had previous myocardial infarction, whereas 20 per cent of the controls had such a history. Since both increasing age and previous infarction[2, 3] are known to be associated with increased mortality, our 0.2-gm.-quinidine-treated group is unfairly "loaded" in favor of a lessened death rate. A possible mitigating factor is the fact that 30 per cent of the 0.2-gm.-quinidine-treated group were females as compared with 15 per cent of the controls. Some writers[3] report a higher mortality in females after acute myocardial infarction, whereas others do not.[4]

TABLE 1. *The Incidence of Arrhythmias in Patients Receiving Quinidine and in Controls.*

ARRHYTHMIA	PATIENTS RECEIVING 0.2 GM.	CONTROLS	PATIENTS RECEIVING 0.4 GM.	CONTROLS	PATIENTS RECEIVING 0.6 GM.	CONTROLS
Total in group	66	55	20	20	25	25
No arrhythmias	41	32	10	13	12	17
Premature beats	17	15	6	4	9	7
Absent after treatment	4	—	3	—	3	—
Auricular fibrillation and flutter	6	5	3	2	2	2
2nd or 3rd degreea uriculo-ventricular block	2	3	2	1	3	1

The incidence of various arrhythmias in the treated and control groups with the different dosage schedules of quinidine is shown in Table 1. It will be seen that in approximately one half to two thirds of all treated and control groups no arrhythmia was observed at any time. Rarely occurring premature beats, less than 1 a minute, were not regarded as an arrhythmia.

Premature beats occurring more often than rarely were observed in from about one quarter to one third of treated and control patients in all three dosage schedules. Of the extrasystoles demonstrated by electrocardiogram, approximately two thirds were ventricular and one third auricular or nodal in origin. In the treated patients, quinidine appeared to abolish the premature beats in from one quarter to one half of those who originally had them and was without noticeable effect in the remainder. No one dosage schedule seemed strikingly superior.

Auricular fibrillation or flutter was observed, often transiently, and proved by electrocardiogram in slightly less than 10 per cent of patients. In some cases in the control groups auricular fibrillation was observed to disappear spontaneously; hence it is difficult to be sure of any beneficial effect from the use of quinidine. Auricular fibrillation and flutter were observed to occur in patients while they were receiving quinidine at all three dosage schedules, usually in the early days following the acute infarction. However, the arrhythmia was usually transient, and quinidine seemed to exert some regulating effect. The beneficial effect of this drug in preventing auricular fibrillation or flutter following acute myocardial infarction is difficult to prove and is at best only moderate — at least in the dosages studied.

Auriculoventricular block, of either second or third degree, was observed in 12 cases. In those patients with this condition in whom quinidine was used we found no evidence to suggest that the drug had either a helpful or a harmful effect. Of the 7 patients with this degree of heart block receiving quinidine only 1 died, the remaining 6 showing a return to normal sinus rhythm in the usual few days. Three of the 5 patients with this degree of heart block in the control group died.

In attempting to evaluate the influence of quinidine on mortality, it was found that in the group receiving 0.2 gm. four times a day 18 per cent of the patients died, whereas the corresponding control group had a mortality of 27 per cent. However, when we recall, as was pointed out above, that this quinidine group consisted of significantly younger persons, on the average, with fewer previous infarctions than the corresponding controls, it becomes impossible to attach any significance to the difference in mortality. It seemed more reasonable to combine the cases in the two groups receiving 0.4 or 0.6 gm. of quinidine every eight hours. This would make a sufficient number of cases to have some possible significance. Moreover, in these two groups the control cases are closely comparable to the treated cases in all respects. If this is done we find that the mortality among the patients receiving quinidine was 20 per cent and that in the controls 22 per cent, a statistically insignificant difference.

When this study was initiated it was thought possible that the administration of quinidine after acute myocardial infarction might prevent the occurrence of sudden death that has been shown to be due, — in some cases, at least, — to ventricular fibrillation. We included as instances of sudden death only those patients who had previously been progressing at least fairly well and who were either found dead in bed or were observed to die within one or two minutes. Excluded from this group of sudden deaths were a few patients who were demonstrated at autopsy to have died suddenly from a ruptured ventricle, since the drug could not reasonably have prevented this occurrence. In 6 of the 8 patients included in the "sudden death" group, autopsy was performed and ventricular rupture

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excluded. All 8 patients were males; except for 1 patient with chronic auricular fibrillation, all were known to have had regular rhythm for several days prior to death.

In the 0.2-gm.-quinidine group there were 1 treated patient and 3 controls. Two of 3 control patients were over sixty-five years of age and 1 of these had had two previous myocardial infarcts; hence they were in an inherently precarious condition. However, the fact that only 1 sudden death occurred among the 66 patients receiving this dosage of quinidine suggests the possibility of some protective action.

When we examine the groups receiving 0.4 and 0.6 gm. of quinidine every eight hours (Table 2), a somewhat different situation is seen. There were no sudden deaths among the 45 controls, but there were 2 such deaths with each dosage schedule among the treated patients. All 4 of these men had suffered severe infarctions but were apparently in fairly good condition at the time of death. Three of the 4 died suddenly from the twenty-second to the thirty-first day after their initial pain. Death occurred from one-half hour to six and one-third hours after quinidine had been given. The evidence suggests that the quinidine at these dosage levels may possibly have been responsible for some of these 4 sudden deaths.

Toxic effects from the administration of quinidine were few and relatively mild. With 0.2 gm. every four hours during the day and with 0.4 gm. every eight hours no toxic symptoms or signs were encountered. Of the 25 patients receiving 0.6 gm. every eight hours, 5 exhibited mild toxic symptoms. Two developed mild diarrhea, which disappeared while they were receiving the drug. Two others repeatedly developed uncomfortable diarrhea if the dose of quinidine exceeded 0.2 gm. every eight hours. One patient had some nausea and vomiting, which disappeared when the dose was reduced to 0.4 gm.

In no case did significant widening of the QRS complexes appear in the electrocardiogram after quinidine was given. A few patients with bundle-branch block were treated without incident. In comparing treated and control groups, no significant difference in pulse rate or blood pressure was noted.

TABLE 2. *Cases of Sudden Death from Acute Myocardial Infarction.*

	Sex	Age	Severity of Infarction	Quinidine Dose	Day of Death after Acute Infarction	Interval Between Last Dose of Quinidine and Death
		yr.		*gm.*		
J. M.	M	66	++	....	19*	....
H. C.	M	59	+++	....	10	....
M. D.	M	71	++	....	7*	....
A. K.	M	58	+++	0.2 4 times daily	41	1 hr., 45 min.
E. W.	M	39	++++	0.4 every 8 hr.	31	30 min.
J. C.	M	65	+++	0.4 every 8 hr.	4	6 hr., 20 min.
J. T.	M	57	+++	0.6 every 8 hr.	27	55 min.
W. F.	M	41	++++	0.6 every 8 hr.	22	3 hr., 40 min.

*No autopsy.

Summary and Conclusions

Quinidine apparently has some action in reducing the incidence of arrhythmias following acute myocardial infarction, but this effect is inconstant and of moderate degree only.

No evidence was obtained that the routine use of quinidine in acute myocardial infarction influences the mortality rate.

The routine use of quinidine in this condition does not prevent sudden death and at higher dosage levels may possibly add somewhat to this hazard.

Toxic effects from the use of quinidine in these dosage ranges are infrequent and of slight degree.

This study offers no support for the *routine* use of quinidine after acute myocardial infarction.

We are indebted to Drs. Charles L. York, Wilbur B. Manter, John A. Kinczel, Raymond L. Dross, C. Warren Irvin, Jr., and Harold L. Godwin for their carefully recorded daily observations and to Dr. William J. H. Fischer, Jr., for his help during part of this study.

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ABDOMINAL PREGNANCY SECONDARY TO RUPTURE OF ACCESSORY UTERUS WITH SURVIVAL OF MOTHER AND INFANT*

Report of a Case

GEORGE A. BOURGEOIS, M.D.,† AND MORRIS W. SHAPIRO, M.D.‡

BOSTON

IN the case herewith reported a living infant was obtained by operation from the mother's abdominal cavity at term, and there is good evidence that fertilization was accomplished by transperitoneal migration of the spermatozöon. Because of the uncertain quality of the uterine scar from this operation, a subsequent pregnancy was terminated by cesarean section. Correlation of the findings in this case with a nonpregnant uterus unicornis unicollis with attached sessile accessory uterus offers an explanation of the pathogenesis.

CASE REPORT

A 24-year-old secundigravida in the 39th week of gestation was first seen on September 15, 1946, because of nausea, vomiting and pain in the right side of the abdomen since the 3d month of pregnancy. She had been admitted to a local hospital for these symptoms on May 23, 1946, at 4½ months' gestation. Examination there showed the fundus to be the size of a 4½-month gestation, with tenderness over the right uterine cornu extending into the right flank and costovertebral region. During 8 days in the hospital her temperature ranged between normal and 100°F. Laboratory examination revealed a red-cell count of 3,130,000, a hemoglobin of 60 gm. and a white-cell count of 13,700. Catheterized urine showed a slight trace of albumin and a sediment full of bacteria but free of pus; the culture yielded no growth. The patient was discharged on May 31, 1946, with a diagnosis of pregnancy, pyeloureteritis and secondary anemia.

FIGURE 1. *Flat Abdominal Plate Taken a Few Hours Before Operation.*

The fetus is shown lying entirely to the left of the midline and presenting by the breech.

The symptoms persisted and became severe, with increased vomiting, 3 weeks prior to admission to the Carney Hospital on September 15, 1946. Her last menstrual period had occurred in December, 1945, the exact date being unknown; there had been no bleeding or staining since. There had been moderate urinary frequency but no nocturia or dysuria.

The patient had had scarlet fever in childhood. She had been operated on for a strangulated left inguinal hernia in 1942. She had been married for 2 years. The first pregnancy had terminated spontaneously at 34 weeks' gestation in June, 1945. It had been complicated by pain in the left flank and renal involvement. The child is living and well. The menarche had occurred at 12 years of age. The periods approximated a 28-day cycle, lasting 7 days. The patient had never had any menstrual pain. Her mother died of "goiter and pneumonia"; the cause of her father's death is unknown. There were no siblings.

The patient had had no headaches and no visual disturbances. There had been no cardiorespiratory symptoms. She had experienced occasional episodes of constipation.

Physical examination disclosed a well developed, pale, apprehensive woman with warm dry skin and dry coated tongue. The blood pressure was 120/60, the pulse 100, the respirations 20 and the temperature 98.6°F. The abdomen was distended to within 2 fingerbreadths of the xiphoid and showed a healed left inguinal incision; it was tender throughout, but especially in the left upper quadrant. There was no spasm and no costovertebral tenderness. The fetal heart rate was 136 in the left flank; there seemed to be a vertex presentation. There was no peripheral edema. Laboratory examination revealed a red-cell count of 3,320,000; a hemoglobin of 60 gm.; a white-cell count of 14,400 with 81 per cent neutrophils, and an essentially normal urine.

Treatment consisted of sedation and intravenously given fluids with vitamins, and nothing by mouth. For 2 days there was no improvement, and it was thought that delivery was indicated. A medical induction was apparently successful, with severe pains at 3- to 4-minute intervals. However, it was noted that uterine contractions could not be felt. After about 8 hours of such "labor" with inadequate rectal findings, a sterile vaginal examination was made. It showed a long, thick, firm cervix admitting one finger. The presenting part was irregular and soft and seemed to be a breech, although it could not be palpated directly. The pelvis was gynecoid-android in type. X-ray examination revealed a fetus presenting by breech and lying entirely to the left of the spine (Fig. 1).

In view of these findings and the patient's failure to improve with conservative therapy, abdominal delivery was decided on.

The patient was seen in consultation by Dr. Roy J. Heffernan, who listed his preoperative choice of diagnoses as abdominal pregnancy and ovarian cyst. We had made the same diagnoses, but in the reverse order.

Operation was performed under nitrous oxide, oxygen and ether anesthesia. Sterile vaginal examination disclosed a long, thick cervix that easily admitted one finger. No presenting part or secundines were palpable. The cervix was displaced to the left by an ovoid mass, firm and apparently extrauterine, that extended from the pelvic brim to the level of the umbilicus.

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‡Assistant professor of pathology, Tufts College Medical School; pathologist-in-chief, Carney Hospital.

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The infant presented by breech, on the left side. The urinary bladder was emptied by catheter.

The peritoneal cavity was opened through a midline suprapubic incision. The parietal peritoneum was injected and adhered loosely to a large bluish-purple friable placental mass. The adhesions of this mass to surrounding structures, — parietal peritoneum and bowel, — were easily separated with less than moderate bleeding by blunt dissection. A broad pedicle in the area of the right infundibulopelvic ligament and a smaller pedicle extending to the small bowel were noted. In the course of this separation a cavity was broken into at the upper pole of the mass; the umbilical cord presented, and a living male infant (weight 6 lb., 2 oz. — 2793 gm.) was extracted by the breech. The liquor amnii was dirty-green but odorless.

The broad, solid pedicular attachment of the placental mass, extending from the right cornu of the uterus to the right round ligament and bearing on its posterior surface an apparently normal tube and ovary, was divided between serially placed clamps, which were replaced with suture ligatures. There was no gross communication between the mass removed and the cavity of the remaining uterus. The firm pedicle connecting the placental mass to a loop of small intestine was divided between two Kelly clamps, the clamp on the intestinal stump being replaced with a suture ligature. The entire mass, consisting of placenta, uterine tissue and the right tube and ovary, was then removed.

A large, thick, red and fibrous sac extended throughout the left upper quadrant and epigastrium. It was firmly adherent to the anterior and lateral parietal peritoneum and enveloped the stomach. About 200 cc. of soft dark-green material resembling milk curd was removed from this sac. Except for the excision of a small piece from the anterior parietal peritoneum for pathological examination, it was not disturbed.

The right peritoneal gutter contained a thin-walled cystic mass from which clear gelatinous material exuded; this material was removed. The residual uterus was approximately the size and contour of that of a 2½-month pregnancy with no opening into the uterine cavity along the line of suture on the right. The sigmoid was adherent to the left pelvic wall by a broad attachment and could not be brought into the pelvis. No omentum was found. A rubber-tissue drain was placed in the cul-de-sac and brought out through the lower pole of the abdominal incision; a second drain was placed in the cavity in the left upper quadrant and brought out through the upper pole of the abdominal incision; a third drain placed in the right peritoneal gutter was brought out through a stab wound in the right flank. The peritoneum and transversalis fascia were approximated with a continuous suture of No. 00 chromic gut. Because of the patient's precarious condition, the remainder of the abdominal wall was approximated with interrupted through-and-through sutures of heavy Dermalon; intermediate skin sutures of fine Dermalon were placed between the deep sutures. The patient left the operating room in fair condition.

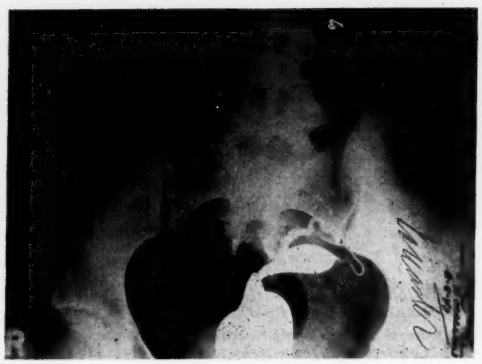


FIGURE 2. *Hysterosalpingogram Made on February 2, 1947, Four and One-Half Months after Delivery.*

A uterus unicornis unicollis is seen. Stereoscopic views of this and companion x-ray plates show that the tube is normal and that its fimbriated end does not connect with the uterus, as suggested by the view reproduced here.

A severe postoperative febrile reaction lasted 2 days, subsiding by the 5th postoperative day. During this period, in addition to the usual supportive therapy, the patient received 1500 cc. of whole blood and penicillin and sulfadiazine. On the 6th postoperative day a large amount of decidual tissue was passed by vagina. On the 8th postoperative day all drains were removed; 5 days later the patient developed a fever that reached 102.6°F. On the 27th postoperative day a tender rounded mass appeared at the left of the umbilicus. During this period the patient received three 250-cc. blood transfusions and another course of penicillin and sulfadiazine. Within 4 days the temperature was normal and the mass became softer and less tender. The patient continued to improve and was discharged from the hospital on November 2, 1946.

FIGURE 3. *Bisected Maternal Surface of Specimen, Showing Placenta* (P) *Attached to Ruptured Accessory Uterus* (U) *with Normal Tube* (T) *and Ovary* (O).

The portion of placenta below the uterus (U) *had implanted itself to the anterior abdominal wall and to a loop of small intestine.*

During the next month night sweats were experienced and the mass reappeared at the left of the umbilicus. However, the temperature remained normal, and by the end of the month both the night sweats and the tender mass had subsided. The patient had a normal period beginning on November 12, with moderate flow but no clots or cramps. With her period, however, there was severe pain in the left side. There were no urinary or bowel disturbances. The abdominal incision was well healed.

A hysterosalpingogram (Fig. 2) made on February 2, 1947, was consistent with a uterus unicornis unicollis with a normal left tube.

By March, 1947, the only complaint was insomnia. The abdominal incision had healed and no abdominal masses were felt. The abdomen was tympanitic throughout. On pelvic examination the uterus was normal in size, contour, position and mobility. There were no adnexal masses or tenderness. The patient was then seen at 3- or 4-month intervals; her periods were regular and painless, and the pelvic findings were likewise normal.

At birth the infant showed a moderate right torticollis, which was successfully corrected by conservative management. The hair was patchy and sparse at the time of birth; it is now normal. The infant is now normal in appearance and development.

The pathological report was as follows:

"Specimen 1 is a placenta with a tripartite form measuring 15 x 15 x 6 cm. (Fig. 3). The attached cord is inserted near one margin and measures 30 cm. in length and 1.2 cm. in diameter; it has three adequate vessels. No amniotic sac is identifiable. The fetal surface of the placenta, except for its trilobular character, appears regular. The material surface of the placenta is, in part, firmly attached to a smooth glistening sheet of tissue. This sheet measures 10 x 8 cm. and varies in thickness from 2.0 cm. in the central portion to 0.1 cm. at its periphery. A patent fallopian tube, measuring 7 cm. in length and 1 cm. in diameter, together with an ovary and round ligament are all attached to this sheet. Sections through the ovary reveal a round corpus luteum 2.5 cm. in diameter, and sections through the smooth sheet of tissue reveal a loose vascular interior with a firm muscular attachment to the maternal surface of the placenta. This tissue resembles myometrium. Sections through the placenta proper reveal several small infarcts about 2 cm. in size.

"On microscopical examination the placenta is composed of well vascularized mature chorionic villi showing small areas of infarction. The attached muscular wall, representing myometrium, shows hypertrophy and hyperplasia; the tube and ovary are free of disease, the corpus luteum being normal.

"Specimen 2 consists of a second small pinkish-gray piece of tissue 1 cm. in diameter removed from the anterior parietal peritoneum.

"On microscopic examination the section of parietal peritoneum shows an abundant granulomatous foreign-body giant-cell reaction to fetal hairs that are imbedded in this area.

"*Diagnosis:* Mature tripartite placenta and cord attached to a muscular wall; healthy tube and ovary with corpus luteum of pregnancy. The peritoneum shows a foreign-body giant-cell reaction to imbedded hair."

The patient's last period before her third pregnancy began on August 19, 1950. Her course throughout was normal, except for two attacks of acute cholecystitis, for which she was hospitalized on January 13 and March 12, 1951. Both attacks subsided with conservative treatment. Because it was not known how badly the myometrium was scarred from the delivery of her abdominal pregnancy and because her first pregnancy had terminated spontaneously and prematurely at 34 weeks' gestation, it was considered advisable to deliver the patient by cesarean section at about 37 weeks.

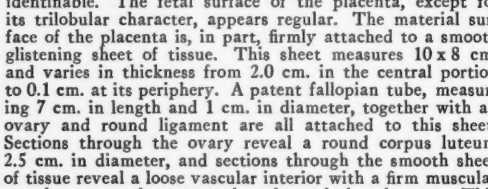


FIGURE 4. *Photograph Taken at Operation on Uterus Unicornis Unicollis.*

The dressing forceps are pointing to the linear depressed vertical scar just lateral to the right end of the transverse cervical incision. The uterus has been rotated counterclockwise so that the normal left tube and ovary are seen at the left, below the dressing forceps.

A transverse cervical cesarean section was performed on May 3, 1951. A living female infant weighing 5 lb., 11 oz. was delivered. This infant cried spontaneously but was deeply cyanosed and died on the 3rd postnatal day. Postmortem examination showed typical congenital alveolar dysplasia with a complicating pneumonia. The uterine cavity was inspected before closure and found to be clean. Palpation and inspection of the right side of the uterus showed no defect in the interior surface of the uterine wall suggestive of an opening to the accessory uterus removed in 1946. There was, however, a linear depressed scar on the serosal surface of the uterus just lateral to the transverse incision (Fig. 4), and in this area there was definite thinning of the myometrium. In view of the patient's last operation, it was notable that the only adhesions present were in the area of the neck of the gall bladder, which was tense and thin-walled and did not empty with moderate pressure. As the omentum was brought down, a large hiatus was discovered in it, and on the left side an irregular nodular, brownish-gray mass approximately 3 cm. in diameter was noted. The nodule was excised and the defect in the omentum closed with interrupted sutures. The patient withstood this operation well, had an afebrile postoperative course and left the hospital on the 10th postoperative day. She was last seen on December 17, 1951, at which time she had no complaints and the uterus was well involuted.

The pathological report made after the operation of May 3, 1951, was as follows:

"The specimen consists of a mass of fatty tissue measuring 5 x 3 x 5 x 2 cm. in the center of which is an irregularly lobular, firm mass, yellowish to reddish-brown in color, smooth on the surface except for a puckered area of adhesions. This measures 1.5 cm. in diameter and on cut surface is a reddish-brown to yellow in color, showing areas of hemorrhage. The tissue is smooth but somewhat friable, and is encapsulated.

"Microscopical examination shows a portion of omentum with a well demarcated area of old hemorrhage and hyalinization, with foci of calcification, and shadowy outlines of infarcted chorionic villi."

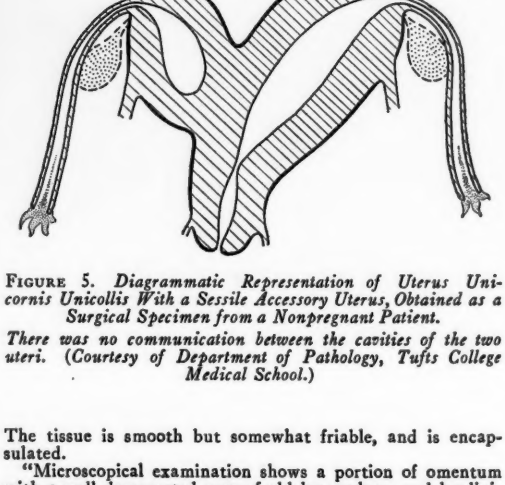


FIGURE 5. *Diagrammatic Representation of Uterus Unicornis Unicollis With a Sessile Accessory Uterus, Obtained as a Surgical Specimen from a Nonpregnant Patient.*

There was no communication between the cavities of the two uteri. (Courtesy of Department of Pathology, Tufts College Medical School.)

DISCUSSION

There was no evidence of a communication between the cavities of the left uterus unicollis unicornis and the right accessory uterus through which a spermatozoön might have traveled. A microscopic opening would have been demonstrated by the hysterosalpingogram; however, none was seen, and there was no suggestion of an opening either on inspection or on palpation of the uterus at subsequent

cesarean section. Furthermore, the location of the accessory uterine tissue as demonstrated at the subsequent section indicated that the existence of an asymmetrical bicornuate uterus was unlikely. If the cavities of the left uterus unicollis unicornis and the right accessory uterus were separate, fertilization of the ovum from the right ovary was accomplished by transperitoneal migration of the spermatozöon after passing through the left tube.

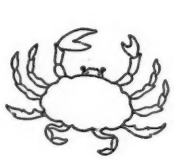
An anomalous uterus obtained as a surgical specimen from a nonpregnant patient by the Department of Pathology at the Tufts College Medical School appears to be similar to that of our case and offers the most plausible explanation for the pathogenesis of the condition found in the case reported herein. This specimen consists of a uterus unicornis unicollis with a small attached sessile accessory uterus (Fig. 5). Both gross and microscopical serial sections of this specimen showed that the endometrial cavity of the accessory uterus had no connection with the endometrial cavity of the uterus unicornis unicollis. Each uterus was associated with a normal tube and ovary. This specimen, the result of incomplete fusion of the müllerian ducts during embryonic life, is considered comparable to the anomalous uterus of our patient.

In the case reported herewith, nidation for the first pregnancy took place in the uterus unicornis unicollis and gestation terminated in premature labor at thirty-four weeks. In the second pregnancy (with a corpus luteum in the right ovary), nidation occurred in the accessory uterus on the right. Since no communication between the endometrial cavity of the uterus unicornis unicollis and that of the accessory uterus could be demonstrated by hysterosalpingogram or by inspection and palpation at subsequent cesarean section, the fertilizing spermatozöon must have successfully accomplished transperitoneal migration. Rupture of the accessory uterus, with an undetermined amount of bleeding and extrusion of the products of conception into the peritoneal cavity occurred between the third month of pregnancy, when the patient first experienced nausea, vomiting and pain in the right side of the abdomen, and the fourth or fifth month of gestation, when she was hospitalized for these symptoms. The clinical symptoms were probably caused initially by small amounts of blood irritating the peritoneum and later by the growth of fetal hair into the peritoneum of the upper abdomen, with consequent foreign-body cell reaction. Since it is unlikely that fetal hair would penetrate an intact amnion, it is assumed that at some time during this process rupture of the amniotic sac occurred. The placenta developed a partial attachment to the anterior abdominal wall and one loop of the small bowel, but it obviously derived most of its blood supply from its attachment to the ruptured accessory uterus.

Summary

A full-term abdominal pregnancy secondary to rupture of an accessory uterus is presented. At laparotomy a living male infant was delivered and the placenta, which derived its principal blood supply from a small accessory uterus on the right, was removed, together with the accessory uterus and its attached right tube and ovary. Both mother and infant (apparently normal) survived. The pathological specimens obtained are described. A hysterosalpingogram was typical of a uterus unicollis unicornis and showed no evidence of a potential communication with the accessory uterus that had been removed. At subsequent cesarean section there were no gross findings, either by palpation or by inspection, to suggest an opening. The corpus luteum of the abdominal pregnancy was in the right ovary, adding further evidence in favor of the belief that the spermatozöon responsible for this pregnancy accomplished transperitoneal migration.

Correlation of the findings in our patient with a uterus unicornis unicollis with an attached sessile accessory uterus — a surgical specimen from a nonpregnant patient — suggests the pathogenesis of the secondary abdominal pregnancy.



PERIPHERAL NEUROPATHY AND SEROUS MENINGITIS DUE TO HORSE SERUM*

Report of a Case With Failure to Respond to Cortisone

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REACTIONS due to horse-serum sensitization, so common prior to the present era of specific antibiotic and chemotherapeutic agents, are now comparatively rare. We are therefore reporting a case of peripheral neuropathy due to tetanus antitoxin in order to re-emphasize the existence of the syndrome and especially to point out the failure of cortisone therapy.

CASE REPORT

A 27-year-old construction worker was admitted to the Brooklyn Veterans Administration Hospital on May 22, 1950, because of fever of 6 days' duration, together with urticaria and pains in the neck and arms for 12 hours.

The patient stated that on May 10, 1950, he had cut his left fourth finger on a galvanized wire fence. Two days later it became reddened, swollen and tender. Boric-acid soaks gave only slight relief. On May 16 he was treated in the Emergency Room of another hospital, where he was given penicillin intramuscularly in the right arm and 1500 units of tetanus antitoxin in the left.

About 3 hours later he developed right-sided chest pain, weakness and frontal and bitemporal headache. He was examined in the Admitting Service of this hospital, where his oral temperature was found to be 100°F. but no other physical findings were noted, and he was sent home. On that same evening he noted alternating warm and chilly sensations and had a moderate diaphoresis. On the next day there was pain, redness and itching at the site of the antitoxin injection. His private physician recorded an oral temperature of 101°F. and incised the purulent area on the finger. The patient was told that he had serum sickness and took 18 antihistamine tablets over a 36-hour period, without relief of symptoms. The itching increased, the temperature persisted at 98 to 100°F., with sweating and weakness, and pains developed in both axillas. A rash appeared over the chest on May 21.

On May 22, 6 days after the antitoxin injection, the patient developed moderate pains in the thighs and severe pains in the outer surface of both arms, radiating to the cervical spine. The rash spread over the entire body.

A physician gave him 450,000 units of penicillin intramuscularly and referred him for admission.

In June, 1938, the patient had sustained a compound fracture of the right radius and ulna, at which time he was given 1500 units of tetanus antitoxin intramuscularly.

He served in the Armed Forces from June, 1941, to August, 1944. During the Sicilian campaign of 1943 he developed a cerebral concussion from bomb bursts in his foxhole, followed by combat fatigue, for which he was eventually discharged from the Army in 1944. It is significant that numerous neurologic examinations were negative, with the reflexes described as "hyperactive." He received tetanus toxoid several times during his military service, without complication.

In January, 1949, he was admitted to another Veterans Administration hospital for spontaneous right pneumothorax, which subsided on bed rest alone.

Physical examination on the night of admission revealed an acutely ill man, writhing in pain. The temperature was 101.2°F., the pulse 100, the respirations 24 and the blood pressure 140/70. There was marked injection of the conjunctivas and generalized giant urticaria. The chest and abdomen were negative. There was a healed laceration on the fourth left finger. He was given an infusion of 1000 cc. of 5 per cent glucose in saline solution intravenously and 0.3 mg. of epinephrine and 64 mg. of codeine subcutaneously.

By the following morning he had improved considerably. There was some infraorbital edema and one urticarial wheal on the left side of the neck. Temperature, pulse and blood pressure were normal. There was questionable flattening of the right side of the face. The pupils were round, regular and equal, reacting to light and accommodation, directly and consensually. The fundi were negative, as were the ears and nose. The tongue deviated slightly to the right, but this was thought to be due to dental abnormality.

There was slight resistance to movements of the neck, but the Kernig and Brudzinski signs were negative. The chest, abdomen, genitalia, rectum and prostate were normal. Each axilla contained a nontender firm nodule measuring about 2 by 2 by 2 cm. There was some diminution of flexion and extension at the right elbow, but all other muscular movements appeared satisfactory. The biceps, triceps and supinator reflexes on the right were absent; on the left, the triceps was absent and the biceps and supinator were +; the other reflexes were physiologic. The tentative diagnosis was serum sickness and possible peripheral neuritis.

He was started on Pyribenzamine, 150 mg. a day, with barbiturates. A 500-cc. infusion of 5 per cent dextrose in saline solution, with 500 mg. of procaine added, gave symptomatic relief.

That afternoon and evening, after the completion of the infusion, he manifested severe distress moaning and crying and complaining of severe pain in the shoulders, for which he required Demerol. His rectal temperature rose to 100°F.

On the following day, May 24, he seemed generally better but was experiencing definite weakness in the right shoulder and right elbow and had slight neck and shoulder pain when moved.

Examination revealed weakness of both shoulder girdles and some flattening of the right deltoid muscle. Occasional fasciculations were seen. The right shoulder could be abducted only 40°, the left 50°. There was beginning atrophy of both infraspinati and diminished flexion and extension at both elbows. The reflex changes were as previously noted, and flattening of the right nasolabial fold was again observed. Sensation was slightly diminished in the axillary-nerve area over the right deltoid muscle and outer aspect of the right arm.

A lumbar puncture revealed clear fluid under an initial pressure of 8 cm., showing a cell count of 133 lymphocytes, a trace of globulin, a protein of 98.5 mg. per 100 cc., a sugar of 55.1 mg. per 100 cc. and chlorides of 125 milliequiv. per liter. No organisms were demonstrated on culture or stain of the sediment, and the complement-fixation test for syphilis was negative. The colloidal gold test was reported as 5.5-7-6-7-8-10-10-10.5-9-8, giving a "C" (meningitic) reaction.

The Pyribenzamine dosage was increased to 600 mg. a day; the patient also received 20 mg. of thiamine chloride orally and 2 cc. of vitamin B complex ("Solu B") intramuscularly each day. He required frequent injections of Demerol to relieve his pain. On the following day his condition was worse. There was marked tenderness over the brachial plexuses. The right deltoid could not be moved actively. The activity of the right trapezius was estimated at +++, of the right biceps and triceps ++, of the left biceps and triceps +++ and of the left deltoid +. Wrist and hand motions were normal. In addition to the hypesthesia over the outer aspect of the right arm, diminished sensation had now appeared over the palmar surface of the first, second and third fingers of the right hand, consistent with involvement of the sensory branch of the median nerve.

On May 24, the heterophil-antibody titer in the blood was reported as 1:896; no agglutination was observed after

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adsorption with suspensions of guinea-pig kidney and ox red-blood cells. Because of the continued progression of the disease the patient was started on a dosage of 50 mg. of cortisone intramuscularly twice a day. The cortisone was continued for 10 days, during which he did not feel well. He required intravenous glucose-procaine infusions or Demerol for relief of his neck and shoulder pain. There was severe anorexia and frequent nausea and vomiting.

After 100 mg. of cortisone had been given, there seemed to be some improvement in the left deltoid and right biceps. The sensory changes in the right hand, however, were aggravated, and hypesthesia was detected in the right forearm for the first time. The neurologic picture gradually worsened during the course of the cortisone therapy, with both deltoids becoming completely paralyzed and marked weakness appearing in both biceps and both triceps. Hypesthesia appeared over much of the right arm and forearm, so that no definite nerve segments could be outlined.

The eosinophil count on the fifth day of the therapy was: before cortisone 231, 1 hour after cortisone 297, 2 hours 319, 3 hours 297, 5½ hours 264 and 6½ hours 253.

A repeat spinal puncture, performed on June 1, revealed 2 lymphocytes, a protein of 49.9 mg. per 100 cc., a glucose of 75 mg. per 100 cc. and a negative reaction for globulin. A culture was negative. Agglutinations for heterophil antibody in the spinal fluid were also negative.

After the 10-day regimen of cortisone had been completed, the patient was given vitamins and various physical-medicine modalities. The pain in the shoulders persisted until June 10, and his weight gradually fell to 137 from its admission level of 147. On June 15 the heterophil-antibody titer in the blood fell to 1:224, with, again, complete absorption by guinea-pig and ox red-blood-cell suspensions. The patient remained in the hospital 4 months longer. During this time he developed marked atrophy of the deltoids, supraspinati and infraspinati. The deltoids remained functionless, but the elbow motions gradually returned to normal. The sensory changes were unchanged on the right; some hypesthesia developed in the left hand. The patient was discharged on October 10, 1950.

He returned for follow-up examination in May, 1951. At this time he stated that he had had no symptoms since discharge. At first he could only work as a truck driver, but later he developed enough strength to assume his old job as a steel-construction laborer. In this latter employment, he noted inability to lift the steel beams as well as his fellow employees and said that this was especially true of motions at the left shoulder. Examination revealed marked atrophy of the left deltoid and the right supraspinatus and infraspinatus. All motions in the extremities were satisfactory, except that with moderate resistance from the examiner the patient could not abduct at the left shoulder. The right triceps and biceps reflexes were still absent. There were no sensory changes.

Discussion

Neuropathy due to horse serum is a fairly distinct clinical entity, although many features of it are as yet unclear. Serum sickness was formerly a common sequel to standard methods of therapy for infections with pneumococcus, streptococcus and meningococcus, approximating 30 per cent.[1] On the other hand, many larger series make no mention whatever of the neurologic complications — such as the monograph by Von Pirquet and Schick in 1905[2] and Goodall's series of 3500 patients in 1918.[3] The first case was probably reported by Vincent and Richet in 1911[4] and in the English language by Dyke in 1918.[5] The syndrome has been described much more frequently in the French literature of the 1920's and 1930's,[6-9] and scattered reports have appeared in the English and American literature.[10-14] Doyle has given an excellent review of the subject,[15] and Lhermitte has compiled a thorough bibliography.[16] The patients affected may or may not have had a previous sensitization with horse serum, and reactions are more likely to occur in those with an allergic background.[1] Characteristically, they develop pain in the extremities four to fourteen days after the therapeutic injection of serum or vaccine. In certain cases the neurologic syndrome is preceded, as in this case, by the fever, arthralgia and adenopathy of serum sickness. At first there are no definite signs referable to the nervous system, even though the pain may be severe enough to require morphine.[11] Only when weakness sets in is attention drawn to the possibility of a neuropathy.

The majority of the patients have signs referable to the *upper trunk of the brachial plexus*, with roots derived from C_5 and C_6, involving the axillary and suprascapular nerves. Bourgignon[17] stated that different nerves are involved by different toxic substances (such as lead and toxin of diphtheria), according to the chronaxie of the muscles they innervated, and his studies suggest that horse serum affects those nerves that innervate muscles of low chronaxie. The role of this electrical reaction is unclear.

However, it must be emphasized that although this Erb–Duchenne type of brachial-plexus lesion is the most common, neurologic changes are seen elsewhere. The lower extremities may be affected. The patient may also have headache, insomnia and pains in the abdomen and spine, suggesting that the process is systemic. There are occasional reports of patients with papilledema[12] and cranial-nerve palsies.[6, 12] One report describes a patient who developed tetanus and was successfully treated with antiserum, only to succumb later to what seemed to be horse-serum sensitization. The terminal clinical course was that of convulsions, multiple palsies and rapidly developing intracranial pressure. Autopsy revealed engorgement of the cerebral vessels, perivascular edema, an organized infiltrate in the lumbosacral meninges and infiltration of the sciatic nerve by fusiform cells of Schwann-sheath origin.[6]

Few writers, however, emphasize that this syndrome may be a generalized reaction in the central nervous system.[18-26] Sheldon[21] noted a "serous meningitis" occurring after tetanus antitoxin, and a few others mention stiffness of the neck or abnormal spinal-fluid findings.[19] DeLavergne and Abel studied the spinal fluids of a group of 20 patients who had lumbar punctures in the course of treatment for horse-serum reactions. The authors noted a lymphocytosis of 5 to 28 cells, increased protein, a trace of globulin and sometimes a lowered glucose.[22] The findings in our patient parallel theirs.

In 1936 Stuart and his co-workers[23] showed that agglutinins to sheep red-blood cells — called "heterophil" agglutination — could be demonstrated in the blood of patients with serum reactions and in-

fectious mononucleosis and in certain normal persons. They further noted that the agglutinins in these three groups could be distinguished by the adsorption with cell suspensions of guinea-pig kidney and ox erythrocytes, as follows: the antibody of normal serum is adsorbed by guinea-pig kidney but not by ox red-blood cells and that of infectious mononucleosis is adsorbed by ox cells but not by guinea-pig-kidney suspensions; the heterophil antibodies of serum sickness are adsorbed by both suspensions.

Our patient developed a titer of 1:896, which was completely adsorbed. When we noted this high titer, we tested the spinal fluid for such antibodies but found no agglutination. Experimentally, it is difficult to make Forssman antibodies cross the spinal-fluid barrier. The presence of heterophil antibody in the spinal fluid of a patient with horse-serum reactions has not previously been reported, although it seems that the heterophil antibodies of infectious mononucleosis are apparently detectable in the spinal fluid of patients with central-nervous-system complications of that disease.[24,25]

The pathology of nervous-system reactions to horse serum is obscure. The common ectodermal origin of skin and nervous tissue has led some authors to postulate urticarial wheals about the peripheral nerves, with subsequent compression and myelin degeneration[8, 12]; others have suggested an antigen-antibody reaction (such as an Arthus phenomenon) within the nervous tissue itself.[21, 26] The idea that this mechanism might be the common denominator was strengthened when reports appeared of peripheral neuropathy due to other agents, such as rabies,[27] cowpox,[28] pertussis,[29] typhoid[30] vaccines,[27] sulfonamides[31, 32] and penicillin,[33] and was supported somewhat by the experimental studies of Rich and Gregory. In 1943 these authors injected sensitized rabbits with horse serum and were able to produce what they considered a typical picture of periarteritis nodosa.[34] They then reviewed autopsy protocols of patients who had been diagnosed as periarteritis and noted that a large percentage had had treatment with horse serum or sulfonamides or both. Their studies suggest that patients with horse-serum nervous-system sensitization have an arteritis of the *vasa nervorum*, but histologic proof is not as yet conclusive.

The decision to employ cortisone in our patient was based on its known value in other syndromes having an antigen-antibody-reaction mechanism.[35] He received a total of 1.0 gm. over a period of ten days with no immediate or eventual benefit. His prolonged recovery and residual disability approximate that in other patients.[9, 14, 15] The limited supply of cortisone available in 1950 precluded our beginning with larger priming doses in this patient. However, the Arthus phenomenon does not generally respond to cortisone. Knowlton and others[36] observed that cortisone did not prevent the development of nephritis in rats who received anti-kidney serum. Harris and Harris[37] induced horse-serum sensitivity in guinea pigs and rabbits and then attempted to modify the shock reaction and Arthus skin phenomenon by administering cortisone; they reported negative results. To our knowledge, however, this is the first clinical report of horse-serum nervous-system reaction treated with cortisone, although at least 2 other patients have been so treated.[38]

It is to be noted that many millions of service personnel were adequately protected against tetanus by the use of alum-precipitated toxoid, which has an extremely low reaction rate.[39] Experimental studies by Gold and others[40, 41] indicate that a protective titer of antitoxin equal to that produced by 1500 units of tetanus antitoxin — 0.1 unit per cc. — is rapidly attained through both initial and repeated injections of toxoid. This is true even when a booster injection is given five years after the previous one. It is suggested that toxoid be used, wherever possible, to avoid the occasional case of horse-serum reaction.

Summary

A case is reported of a patient who developed peripheral neuritis and abnormal spinal-fluid findings after the injection of horse serum. The failure of response to cortisone is noted.

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MEDICAL PROGRESS

CURRENT TRENDS IN PHYSICAL MEDICINE AND REHABILITATION

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IN the last article of this series of progress reports on physical medicine and rehabilitation it was pointed out that there was a fundamental need for further education of physicians and of the public in aims and possible accomplishments of physical medicine and rehabilitation. To accomplish the desired results the acute need for trained physicians and technical personnel in this specialty had to be met, and facilities available needed expansion. In particular, it was advocated that new rehabilitation centers be established.[1] Although the deficiencies cited two years ago obtained particularly in New England, similar needs are felt in most states. As the training of physicians in this specialty is one of the chief bottlenecks in expansion of the specialty and services to communities, studies have been made to determine what is being done in the leading medical schools of the country to train physicians in physical medicine and rehabilitation. The Advisory Committee on Education of the Council on Physical Medicine and Rehabilitation of the American Medical Association has been conducting surveys on the present state of facilities in our medical schools. They have found that there are 37 schools having departments of physical medicine and rehabilitation, 31 of which have physiatrists on the staff. Forty-five schools do some teaching of the specialty on an undergraduate level, and 17 give graduate courses. Sixteen schools are attempting to develop departments in the near future. Although 67 per cent of the schools do teach either physical medicine and rehabilitation or physical therapy, only 10 schools have separate departments headed by physiatrists. The number of new departments, however, is increasing as more physiatrists become available through residency training programs. At the present time the Council on Medical Education and Hospitals of the American Medical Association lists 43 hospitals offering approved residency training programs with a total of 87 positions for assistant residents and residents. Eleven of these are in the Veterans Administration and 3 in the United States Army. Unfortunately, at least one third of these positions are unfilled, and in view of the necessity of supplying younger men to the Army it seems unlikely that conditions will change materially in the near future.

Successful application of physical medicine and rehabilitation in practice is also dependent on a supply of well trained ancillary personnel. The key members of this team are the physical therapists and occupational therapists. Although there are 31 approved schools of physical therapy, which could turn out a maximum of 683 students a year, and 24 schools of occupational therapy with a maximum possible enrollment of 364, the demand still far exceeds the supply. Some mention should also be made of the rather confusing array of persons who are connected in various ways with the rehabilitation team. In the Veterans Administration, in which these ancillary groups are most highly developed, the different branches are known

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as corrective therapy, manual-arts therapy and educational therapy, in addition to physical and occupational therapy. Probably the greatest confusion is centered around the corrective therapists. These workers are trained in physical education but as yet have no recognized training in relation to treatment of patients through recognized courses in medical sciences. In the Army their work is limited to physical reconditioning in order to prepare soldiers for return to active duty. In the Veterans Administration, however, they are allowed to give exercises and adaptive sports for psychiatric patients and also, in many instances, therapeutic exercises for patients with paraplegia, hemiplegia and other disorders of locomotion or neuromuscular function secondary to disease or trauma. Although they are intended to work only under medical supervision and prescription, many, through years of experience, have become highly skilled and have contributed much to the rehabilitation of these hospitalized patients, in spite of the lack of formal medical education similar to that of physical and occupational therapists.

The manual-arts therapists are limited to Veterans Administration hospitals and are skilled workmen such as carpenters, printers, radio and watch repairers, mechanics and so forth, who under medical prescription teach patients either for direct therapeutic effect, as in the case of the psychiatric patients, or for prevocational analysis and training. The educational therapists, also a product of the Veterans Administration, are schoolteachers who give courses for patients, particularly those with tuberculosis or psychiatric disorders, but also for patients who have been severely handicapped for a long time, such as paraplegics.

There are many other personnel on the rehabilitation team, with even less well defined activities, who are frequently called therapists. Their work includes recreational therapy, music therapy, bibliotherapy and speech therapy. The medical social-service worker and the psychologic tester and rehabilitation counselor are also included as useful aides to those rendering rehabilitation service. There is a great need to know more clearly how many different types of ancillary personnel are valuable for rehabilitation and what their qualifications and training should be for giving treatment under the prescription of the physician. The medical profession must also decide about proper indoctrination in medical ethics and practice. Here again, the Council on Physical Medicine and Rehabilitation and its advisory committees — and also the Council on Medical Education and Hospitals of the American Medical Association and the American Registry of Physical Therapists — are all working diligently on this problem at the present time and will offer a plan for classification in the not too distant future, so that the physician seeking the services of these workers may more intelligently select those with proper qualifications. These groups will also establish a plan for proper training of those seeking to enter the broad field of medical rehabilitation.

In addition to efforts to meet the tremendous need for further education of personnel in the specialty of physical medicine and rehabilitation, it has been possible to improve many existing facilities and to establish new units during the past two years. The most striking example is the new Institute of Physical Medicine and Rehabilitation of New York University and the Bellevue Hospital in New York. Other developments of particular interest to the readers of this journal have occurred on a smaller scale in New England. A new rehabilitation center at the Boston Dispensary, in connection with the New England Medical Center, has been established. A new department of physical medicine has been opened at the Beth Israel Hospital and the department at the Boston City Hospital is also in the process of reorganization and improvement. The Long Island Hospital of the City of Boston is fortunately establishing a new physical-and-occupational-therapy service, and, under the guidance of an able consultant, notable advances are being made in the rehabilitation of supposedly chronically disabled persons. The Community Workshops of Boston is continually improving its facilities so that it can offer greater services in rehabilitation to severely handicapped patients, including vocational training in addition to the sheltered workshop. The Curative Workshop in Worcester, the Bay State Treatment Center in Springfield and the Truesdale Hospital in Fall River are also increasing their activities in rehabilitation.

The opening of the Bay State Medical Rehabilitation Clinic on the grounds of the Massachusetts General Hospital makes available, with the combined facilities of the Massachusetts General Hospital, the only complete rehabilitation center of its kind in New England. It is now possible to admit patients to a hospital physical-medicine rehabilitation service and provide complete medical care including all types of diagnostic and therapeutic procedures, with physical and occupational therapy for patients confined to bed and also physical reconditioning and rehabilitation for seriously handicapped patients such as paraplegics, amputees, hemiplegics and those suffering from infantile paralysis and arthritis. Ancillary rehabilitation services include speech therapy, occupational analysis, prevocational testing and training and psychologic testing and rehabilitation counseling. This service is under the direction of certified physiatrists and residents who are being trained in physical medicine and rehabilitation. Because these complete rehabilitation services are available and because so few beds of this type are available in the country, the Welfare and Retirement Fund of the United Mine Workers of America has se-

lected this center to which to refer severely injured or handicapped members, particularly paraplegics, for complete care. Local insurance companies and practicing physicians and surgeons also are availing themselves of this new type of service for their patients.

Another indication of greater interest in and acceptance of the value of medical rehabilitation is the establishment of a State Rehabilitation Commission, which has the power to determine whether or not proper rehabilitation services are being provided to the injured workman under the Workmen's Compensation Act and may require that these men receive treatment in approved facilities. The insurance companies, who must pay for these services, appear to recognize their value and are seeking this type of treatment for the industrially injured patients to speed their return to industry.

The Literature

One index of the development of a medical specialty is the amount and quality of the medical literature concerned with it. During the past two years a number of books have been published that are worthy of comment. Krusen[2] has edited a general textbook that comprises chapters by some 24 contributors. The entire field of physical medicine and rehabilitation is well covered, including sections on basic principles of physiology as applied to the clinical practice of physical medicine. In England, Cyriax[3] has published a new and completely revised edition of a previous work emphasizing technics and principles of massage and manipulation. These technics are much more commonly applied by physiatrists in England, and there is little in the literature of our country that deals with this subject in any detail. Other texts have appeared on specialized aspects of medical rehabilitation. For example, *Speech Habilitation* by Cass[4] and *Recovery from Aphasia* by Wepman[5] are recommended to those particularly interested in this field. Other books deal with technical aspects of physical rehabilitation. These include a book on ambulation by Dening, Deyoe and Ellison[6] and Buchwald's *Physical Rehabilitation for Daily Living*,[7] which describes in detail the physical treatment of paraplegics. The latter text is notable for its excellent photographs. A monograph has also appeared on the subject of progressive-resistance exercise by DeLorme and Watkins.[8] This reports a technical advance in therapeutic exercise with widespread applications. Other books of interest relate to orthopedic subjects — for example, *Scoliosis* by Kleinberg,[9] *Posture and Pain* by Kendall, Kendall and Boynton[10] and *Cerebral Palsy* by Pohl.[11] The Instructional Courses of the American Academy of Orthopaedic Surgeons[12] as published each year are always of especial value to workers in physical medicine. The text entitled *Orthopaedic Appliances Atlas*,[13] which deals with the history of brace-making and similar appliances, is a particularly valuable contribution to medical literature in this field, as is a new book on orthopedic shoes.[14]

Two new journals have appeared: *The Annals of Physical Medicine*, edited by Hugh Burt, is the official organ of the British Association of Physical Medicine; the former *Occupational Therapy and Rehabilitation* has a new editor and a new title, *The American Journal of Physical Medicine*.

Numerous clinical reports in the literature deal with the use of physical medicine in various medical conditions. Since the advent of ACTH and cortisone in the treatment of rheumatoid arthritis, there has been a renewed interest in the utilization of physical medicine in the treatment of these patients who receive the new drugs. Polley and Elkins,[15] in one of the first reports on this subject from the Mayo Clinic, conclude that clinically there is a need for physical medicine, particularly for patients who have limitation of motion that is reversible by these drugs and who can further their functional recovery by therapeutic exercise. It is also important for patients who because of individual susceptibility cannot tolerate hormones and for those who have irreversible articular changes and require further treatment for correction of deformities and for overcoming persistent muscular weakness or atrophy. There are other patients who could not be candidates for rehabilitation from serious disabilities due to rheumatoid arthritis without the aid of cortisone. Physicians at Columbia[16, 17] have also reported on the value of these drugs and conclude that neither ACTH or cortisone alone nor physical measures alone can yield the benefits gained when drug therapy and physical measures are properly combined. Their statement that physical measures that are strenuous enough to help severe arthritics are impossible without cortisone or ACTH because the rebound effect leaves the patient worse than before might well be reversed in its implications, it appears to the writer — that is, the rebound after withdrawal of drug therapy is likely to be more severe than any rebound effect from medically prescribed and properly administered physical-medicine procedures. Physicians at the Mayo Clinic, where the effects of ACTH and cortisone alone were originally reported, have recently analyzed the results of combining physical and drug therapies. They found that 80 per cent of a group of 34 patients with moderate-to-severe disease showed improvement when treated with only physical medicine and other conservative measures, using as objective measurements as possible. When cortisone was added to physical measures in another group of 54 patients, the percentage increase was only to 85 per cent, which illustrates the fundamental value of physical medicine with or without the addition of steroid preparations. They have also emphasized the importance of individualizing the treatment program,

since the requirements of physical medicine and cortisone vary widely in different cases.[18]

A recent issue of *Rheumatism* is of interest to all those treating rheumatic patients. Erickson[19] has shown how the basic principles of therapeutic exercises can be practically applied in rheumatoid arthritis so that the physician may more intelligently prescribe this important physical procedure for his patients. Another paper[20] in the same issue is noteworthy because of its anatomic and roentgenographic studies of the cervical spine as a cause of shoulder-girdle and arm pain from compression of cervical roots secondary to arthritic changes. Anatomic drawings and excellent x-ray reproductions, including myelographic evidence of root compression, together with a clinical discussion of these entities, are helpful in establishing diagnoses. Little is said about treatment, but those familiar with the syndrome will agree that physical measures including head traction, local use of heat, massage and corrective postural exercises are of proved value. In the same issue Crowe,[21] of Oxford, reports on the benefits of "Trafuril" in the treatment of "muscular rheumatism." Although this diagnosis is not generally accepted in this country, there are certainly many patients who complain of recurrent attacks of localized muscular spasm of the shoulder girdle, trunk and low-back areas seemingly brought on by exposure to cold and aggravated by fatigue and postural strain who may be grouped as a clinical entity. Experience has shown that many types of counterirritant treatments are of value in relieving the muscle spasm that is obvious on careful manual physical examination in these patients. The drug reported on in this paper is related clinically to nicotinic acid and is described as causing an effective hyperemia from local application, which is beneficial in relief of symptoms. It is suggested that application of this drug followed by methods of ion transfer using the positive pole increases effectiveness, particularly when the drug is applied as a tincture. The drug also seems to have some general effect in the relief of pain, but the mechanism is not understood.

Physical-medicine and rehabilitation procedures should be considered in planning the total therapeutic program for patients with chronic degenerative diseases. Among this group the disabled cardiac patient is worthy of mention because of the development of so-called "work classification units" that have been developed in a few centers, particularly in New York and Cleveland. A recent report from the work-classification unit of New York University by Goldwater, Bronstein and Kresky[22] is of particular interest, as they found that a significant number of patients were apparently incapacitated by erroneous diagnoses of heart disease. This signalizes the necessity of utilizing the best of diagnostic procedures and skills before attempting any rehabilitation treatment. The importance of psychologic considerations in rehabilitation of the cardiac patient in industry is also pointed out by Stainbrook.[23] He interprets rehabilitation as the re-establishment of character or reputation or restoration of security or self-esteem. This latter goal is referred to as the chief task in the rehabilitatory management of cardiac disease.

There is an increasing need for attention from the medical profession to the problems of treatment of the aged person. The study of this group is often called gerontology, but, as Moore[24] has noted, this is a subspecialty of many other specialties and requires the co-operation of different groups, including those in physical-medicine rehabilitation. Aside from medical problems, the sociologic aspects of aging are worthy of consideration on the part of the medical profession. Many of these problems have been ably discussed by Randall[25] in a symposium on the subject recently printed in the *Journal of the American Medical Association*. It has been suggested that management take an interest in preparing the employee for retirement; this would, of course, require the help of the medical profession. This is a long-range program[26] with many ramifications, including rehabilitation of workers with chronic diseases, that should provide some means for placement of employees successfully rehabilitated. The personality changes of the aging person have also to be considered.[27] The psychiatrist may be of great aid, first of all, in correctly differentiating the symptoms of mental and emotional changes that are to be expected and those that are evidence of senile deterioration. The physiatrist may play a valuable role in salvaging patients placed in institutions for the aged or for chronic disease who have not had the advantages of possible rehabilitation. The procedures utilized may include a limited amount of physical rehabilitation to improve the degree of independence of the patient, including activities of daily living and locomotion, and also occupational therapy and guidance in limited employment.

Another chronic disease that has received little attention in the literature of physical medicine is Hansen's disease. Some of the most common symptoms of leprosy are related to disease of the peripheral nerves, and physical therapy, including the use of properly designed splints, may be very helpful in the care of these patients. An interesting account of cases referred to the physical-therapy department in the national leprosarium appears in the *Physical Therapy Review*.[28] Although evaluation of the effect of treatment is difficult, it is believed that much can be done toward the prevention of deformities in this disease, which is so very slowly progressive.

Neurologic Conditions

The treatment of patients suffering from diseases of the nervous system constitutes an important part

of the practice of physical medicine and rehabilitation, and various aspects of this broad field have been discussed.[29] One of the most common conditions encountered in general medical practice is that of hemiplegia due to a cerebral vascular lesion. A number of papers discussing in the necessary detail the use of physical and occupational therapy and braces have appeared recently.[30-32] These explain the importance of the prevention of contractures through proper positioning in bed and passive stretching of paralyzed extremities, followed by early attempts at ambulation whenever the patient's general medical condition permits. Some expert advice is usually necessary in order to prescribe proper braces and start the patient on a realistic program. It is possible to do this within the home in many cases if time is spent on the details of instruction. One of the greatest disabilities in those with right-sided hemiplegia is the occurrence of aphasia, and whenever possible language therapy should be included in the physical medical prescription.

The chronic progressive neurological diseases, particularly multiple sclerosis, have received considerable attention lately. Excellent summaries have been published of the present status of medical treatment; of particular value are the publications of Schumacher[33] and Gordon[34] on the utilization of physical medicine in enabling these patients to achieve a maximum of independence and usefulness. Statistics recently accumulated concerning prognosis and life expectancy can be used by the physician caring for these patients to great advantage, as they justify giving the patients considerable encouragement.[35-37]

As might be expected, cortisone has been given a trial in these chronic neuromuscular diseases for which we have no specific treatment. In recent observations on 58 patients it was noted that many undesirable side-effects occurred, including some of the clinical manifestations of Cushing's syndrome, but no significant alterations were noted in patients with progressive muscular dystrophy, myotonia atrophica, Parkinsonism, Wilson's disease and Sydenham's chorea. Patients with amyotrophic lateral sclerosis showed some diminution of fasciculation but no improvement in strength. Thirty-three patients with multiple sclerosis were treated and one third showed some improvement, but the results were only transient. In only 2 patients did improvement suggest an induced remission. There were no definite changes that were regarded as curative, and further investigation seemed indicated.[38]

The problem of caring for the paraplegic patient has already received considerable attention in the medical literature. Although adequate treatment of veterans has been provided through the Veterans Administration hospitals, the care of the civilian paraplegic is still an unsolved problem. One of the largest veterans' centers is at the Hines Hospital in Chicago. An excellent summary of the medical management of these patients has been prepared by their medical team of experts.[39] This includes general principles of medical care as well as physical-medicine rehabilitation technics. Among the new developments in treatment is that of anterior-rootlet rhizotomy, recently described by Munro,[40] who has done much pioneer work in saving the lives of paraplegics.

Cerebral Palsy

Despite advances in preventive medicine, children with cerebral palsy continue to be born, and treating them for the rest of their lives is a problem lying largely within the field of physical medicine and rehabilitation. Our present knowledge on the subject has been carefully summarized by Denhoff, Smirnoff and Holden.[41] Their report includes adequate discussion and reference to the literature on etiology, disturbance of physiology and the clinical problems of ophthalmology, hearing, speech, dentistry, education, psychology, physical and occupational therapy, orthopedic surgery, neurosurgery, and bracing technics. Attention is also called to a new book on the subject by Pohl[11] and to Fuldner's[42] methods of examination of children with cerebral palsy.

Poliomyelitis

The use of physical-medicine procedures in the treatment of poliomyelitis has been well publicized and needs no further comment — except that there are still not enough physical therapists to supply the treatment indicated. Experience has shown the value of more intensive treatment, such as the use of progressive-resistance exercise, even in late cases.[43, 44] Emphasis has also been placed on mechanical aids to further independence of the patients with residual paralysis.[45]

Psychiatric Disorders

The possibilities of utilizing physical medicine in the treatment of patients with various psychosomatic complaints has not been widely utilized or, at least, written about, although some teams of physicians have found it useful.[46, 47] The utilization of the physical-medicine rehabilitation service in the neuropsychiatric hospitals of the Veterans Administration represents a large medical effort. One of the best examples of this is the program of the Veterans Hospital at Northport, Long Island, which has been ably described by Dancik.[48]

Technical Papers and Research

Basic and clinical studies on the effects of microwave diathermy have been continued. Animal experiments have shown that deep thermal destruction of bone and nerves and other structures is possible; so far, no effects have been proved that can-

not be explained by heating of tissue. With proper precaution in prescription and technic of application, this appears to be a useful physical agent.

Ultrasonic energy has been used in Europe for a number of years, with many therapeutic claims for nearly all diseases for which physical therapy is used. Physicians in this country, however, have been more cautious; animal studies have shown that considerable deep heat and necrosis can be caused by ultrasonic radiation.[49] These sound waves have also been used diagnostically to determine the position of the ventricle, thus making in effect a sound ventriculogram.[50] Some investigators have applied ultrasound to a number of clinical conditions with some beneficial effect.[51] It is still, however, not clear how valuable this type of energy will be in the general practice of physical medicine.

Several investigators have reported studies of different aspects of exercise physiology. Hellebrandt and others[52] have noted a significant effect from bimanual exercise on the work capacity in unilaterally weak muscles. Other workers[53] studied the relation of maximum grip strength to strength endurance and found that the development of strength endurance is not directly proportional to the development of maximum strength. Special technics of exercise have been developed by Kabat. Most of the literature on the subject is not easily available (it appears in the *Permanente Medical Bulletin*), but it has been summarized in *Science*.[54] Kabat's special methods are used to develop substitute pathways for voluntary motion by invoking certain facilitative reflex movements. It becomes clear that the performance of muscles can be increased through central facilitation by bringing in synergistic groups and following reflex patterns. Interesting clinical research on this subject was carried out by Hellebrandt and others.[55] The exercise sessions using these technics are as long as two hours and are strenuous for both patient and operator. Considerable manual resistance may be employed; this, of course, has obvious value in strengthening muscles. Such prolonged daily manual treatment of patients must frequently have considerable psychologic effect, which to date has not been evaluated in the medical literature.

The use of progressive-resistance exercise technics as described by DeLorme has been found to have widespread application.[8, 43, 56]

A valuable collection of papers on technics of using crutches and braces for rehabilitation is published in the 1951 volume of *Occupational Therapy and Rehabilitation* and is being continued in the new journal replacing it, the *American Journal of Physical Medicine*.[57] Another paper of practical value discusses the causes and corrections of deviations in gait in the above-knee amputee. This paper is in outline form and is illustrated, thus being valuable teaching material.[58]

The subject of hydrotherapy has not received much attention in recent medical literature. Hellebrandt and others,[59] however, have reviewed the history of the application of hydrotherapy by agitation of water in the so-called whirlpool bath and have developed methods of measuring temperature pressure and turbulence. Little is yet known about the value of these various factors. Spa therapy is more widely utilized in Europe than in this country, and papers on the subject are not readily available here. There is, however, an excellent collection of abstracts in the December issue of *Occupational Therapy and Rehabilitation*.[60]

The effect of physical agents on circulation of the extremities is a most important subject to those in the field of physical medicine. This topic has been studied over a ten-year period by Wilkins and others, and the results of their work have been reviewed and summarized in a paper of fundamental importance to all using physical procedures for treatment.[61] Their studies have to do with the use of heat, posture and pressure cuffs. These investigators have emphasized that reflex sympathetic vasomotor activity can be as important as local vasodilating factors such as direct application of heat in determining blood flow in limbs. They have also pointed out that relief of sympathetic vasoconstriction through warming of the whole body is less dangerous than local heat applications. They also questioned the value of Buerger's exercises and have indicated that in certain patients these are better done passively than actively, as active exercise may unnecessarily increase oxygen demand. They also doubt the value of elevation of the limb above the horizontal and found no evidence to support the rationale of intermittent venous congestion for the relief of ischemia. They did not, however, determine whether this did or did not increase collateral circulation.

Electromyography

The physiatrist is finding that electromyography is an important diagnostic and research method; numerous papers on this subject have appeared in recent literature. Kendell[62] and his associates report some preliminary studies on recording technics, and Arieff and his co-workers[63] have described a portable recording machine. The clinical value of electromyography has been studied by Richardson,[64] who describes abnormalities in different neurologic conditions. Huddleston and others[65] have also discussed diagnostic features of electromyography, as has Watkins.[66] Knowlton and his colleagues[67] have used electromyography to study fatigue in poliomyelitis patients, and other investigators have used these technics to study muscle action in normal and spastic conditions.[68-70] Lion and his associates have developed an ingenious electrical method of measuring muscular activity of eye muscles.[71-73] Although various reports on electromyography have

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appeared, there is still great need for further standardization of technics, so that results from different laboratories and clinics may have more meaning to both investigators and clinicians. This would be a worth-while goal for specialists in physical medicine and rehabilitation, and it is hoped that a future progress report will be devoted to the subject.

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MEDICAL INTELLIGENCE

EXPERIMENTAL PREPARATION W-483 IN THE TREATMENT OF PARKINSON'S DISEASE*

WILLIAM H. TIMBERLAKE, M.D.,† AND ROBERT S. SCHWAB, M.D.‡

BOSTON

THE past six years have seen the development of a number of new synthetic chemicals whose safety in animal experiments has permitted their trial in the treatment of Parkinson's disease. One of them, Panparnit, was introduced in Switzerland by Hartmann[1] in 1946, but his enthusiastic report was not substantiated by other clinical investigators. Sciarra and his colleagues,[2] for example, found the drug to be of no use whatsoever in the treatment of this condition and the report by Schwab and Leigh[3] fell in between these opposite opinions. Extreme divergence of opinion has been characteristic of therapeutic claims in the treatment of paralysis agitans since the original paper by Parkinson[4] appeared in 1817.

A similar disagreement followed the report of Sigwald et al.[5] on the use of Diparcol and the report of Budnitz[6] on the use of Benadryl. An enthusiastic report in a lay journal on the use of Artane was followed by more conservative appraisals by clinical investigators using the same drug. A modification of the chemical formula of Diparcol into a compound known as Experimental Drug W-483§ was reported by Durel[7] in 1949. Both have been used in the treatment of Parkinson's disease. The reasons for the conflicting reports on medical treatment of Parkinson's disease are partially covered in the article by Schwab,[8] and further aspects of this problem will be discussed in this communication. In October, 1950, a supply of Experimental Drug W-483§ was made available for clinical trial. This compound is [Diethyl amino-propyl]-N-dibenzoparathiazine hydrochloride.

METHOD OF INVESTIGATION

The authors are well aware of the difficulty of evaluating results of treatment in Parkinson's disease and have tried to guard against the errors that might occur in an ordinary clinical trial of a new medicine. The drug was tested on two groups of patients of approximately 50 each. Group 1 was composed of outpatients who came to the hospital on an average of once a month by appointment; they were examined in groups. Each patient received approximately fifteen minutes of clinical evaluation by the outpatient physician, and the patient had no further contact with either the hospital or the examining physician until the next visit. Various drugs for combating the symptoms of Parkinson's disease were tried and changed without explanation to the patient, and there was a minimum of laboratory testing, supportive suggestion or psychotherapy.

Group 2 was composed of private patients who were aware that they were coming to a physician's office both for help and for trial of new therapeutic methods. A battery of objective laboratory tests were performed at each visit and were independently scored by technicians. In addition to these tests, described in a previous communication,[8] a neurologic examination was made at each visit and supportive reassurance was stressed. In addition, patients were allowed to telephone or write comments to the physician and were urged to seek additional changes of medication as often as they wished.

W-483 was available in tablets of 10 and 50 mg. each. The tablets were scored so that half-doses were possible. In addition to the tablets, a supply of pure salt was made into a palatable elixir containing 25 mg. per 4 cc. Identical-appearing blank tablets were available when placebo control was desired. No parenteral medication was used in this study.

TECHNIC

W-483 was substituted gradually in increasing amounts for one of the medicines that the patient was already receiving. When the patient was taking W-483 alone, the drug was continued for a trial period before other drugs were added. It was usually possible to reach a satisfactory level of W-483 in two or three weeks and continue on this for a month or two before other changes were made. If undesirable or toxic side-reactions occurred the drug was discontinued promptly, except in a few cases in which a second trial was made with smaller increments of doses. The presence of undesirable side-effects in over half the patients made it necessary to devise a more elaborate technic of administration. The correct form of varying dosage is illustrated in Table 1.

At the end of a six-month observation period an assessment of the effect of W-483 was made in 70 cases. A second assessment was made at the end of a year on 117 patients.

In the Out Patient Department group (42 patients) W-483 when used alone benefited only 4 patients more than other drugs previously administered. In 4 others W-483 had to be supplemented by other drugs. Thus 8 patients out of 42 were benefited by the administration of W-483 — a 19 per cent improvement.

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Aided by a grant from the Warner Hudnut Company, who also obtained the drug in generous quantities for this clinical trial.

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§Designated Parsidol in Europe and Lysivane in the British Commonwealth.

In the private group, in which close supervision and adjustment was carried out, the results were much better. Forty of 75 patients were improved over their previous adjustment. However, only 6 of these were benefited by W-483 alone. Thirty-four took other drugs either to supplement the effect of the W-483 or to neutralize its side-effects. Twenty had to discontinue the drug because of toxic side-effects, and 15 found the drug not so effective as others and therefore discontinued it. Some patients showed continued improvement for eighteen months. With correct adjustment in the first month, increasing tolerance was not evident later. The amount required per day had to be varied from time to time. Hospitalization enabled more rapid and better supervised regulation; favorable results in 12 of 17 cases were noted after observation under these controlled conditions.

The technic of administering the drug advocated by Sigwald is, in some respects, different from that used in the majority of patients in this study. Sigwald believes that the initial dose taken in the morning on awakening should be the largest of the day; in midmorning a dose of approximately one third this amount is given. The after-lunch and mid-afternoon doses are about two thirds of the initial morning dose; the evening dose, taken before retiring, is about one third of the initial dose. He achieves these dose changes by using both the 50-mg. and the 10-mg. tablet so that these exact differences can be followed. This regimen is usually followed without change for five days; he then slightly increases each of the five daily doses and continues for another five-day period. He allows 7 five-day periods to achieve full medication. With 10 patients in our series we followed this technic, achieving success in 6 cases and failure in 4. This is slightly better than our average with our own technic, but it further complicates the schedules, and some patients are unwilling to make these changes during the day.

The private patients consult neurologists by choice and pay a consultation fee for each visit. Unless the medicine given to such patients produces a favorable result, they are likely to consult other neurologists or to return to their general practitioners, whose fees are smaller. Therefore there is a tendency for the patient population to change continually; this leaves a residue of more rapidly benefited patients who continue to visit the physician. Patients with personality defects sooner or later tire of one particular physician and consult another. This is not the rule in an outpatient clinic.

The other difference lies in the personal supervision given by the private physician. In the outpatient group, changes in medication can be handled only at monthly intervals. In the private office, frequent telephone calls, letters or, if necessary, daily or weekly visits can be arranged. Minor changes and alterations in dosage schedules were possible on a much larger scale in physicians' offices than in the outpatient clinic.

A schematic diagram of an example of successful administration of W-483 is shown in Table 1. The important points are: the previous medication on which the patient was adjusted must be maintained for the first two weeks, and during this time the W-483 should be added in very small increments. During the second two weeks the W-483 increment may be increased and the usual or previous medication decreased. During the third two-week period the previous medication is rapidly decreased, while the dose of W-483 is increased further. By the seventh week the patient is on the new medicine alone. In the ninth week the new medicine is reduced if necessary and some of the old medicine may again be added. In the eleventh week some side-effects are specifically neutralized by the addition of a drug such as Dexedrine. Only if this careful adjustment is followed can the best results be obtained with W-483. If such a scheme is not followed, overmedication and undermedication will be experienced in various degrees and an unsatisfactory result will thus ensue.

Table 1. *Correct Form of Varying Dosage.**

First Week	Third Week	Fifth Week	Seventh Week	Ninth Week	Eleventh Week
Artane 4 mg., 4 times daily Small increment of W-483	Small decrement of Artane Large increment of W-483	Small increment of W-483 Large decrement of Artane	W-483, alone, 40 mg., 4 times daily	W-483 Artane	W-483, 25 mg., 4 times daily Artane, 2 mg., 4 times daily Dexedrine, 5 mg. morning and noon
Patient fairly comfortable	Patient feeling fairly well — not so well as previously	Patient feeling better than ever	Patient has slipped back; salivation; unsteady on feet.	Patient much better; slightly drowsy around noon.	Patient still better; excellent result.

*Patient previously given Artane alone.

Discussion

The two groups of patients under consideration were different in type. An outpatient who comes to a large general hospital for medical treatment is usually unable to go elsewhere. Patients with vascular diseases, vulnerable personalities and other concomitant difficulties tend to swell the percentage of unfavorable results in any medical therapy tried.

Summary

W-483, a new medicine for the treatment of Parkinsonism, was tested in 117 patients under various conditions, supervised and controlled for comparison with their previous medication. W-483 was found somewhat difficult to regulate and less useful under outpatient conditions (19 per

cent of patients improved) than when used in private cases. Under regular personal supervision, private or hospitalized patients showed favorable results in 53 per cent of cases. W-483 was most efficient when combined with other drugs.

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NEW CONTRIBUTOR

Dear Editor,

I know you are a medical magazine and wonder if you publish stories about doctors. I thought it might surprize Dad if you could use this one.

Sincerely yours,

Carroll Brownlee

Wellesley, Massachusetts.

My father is a doctor, and it is sometimes a nuisance. Here is an example:

(7:15 a.m. in the doctor's home at the table)

Dad: Good egg, isn't it?

Me: Yes, Dad, and . . .

Phone: Ring — Ring — Ring.

Me: Oh dear.

(Ten minutes later)

Me: Who was that?

Dad: Just a patient. I have to go to Weston right after breakfast.

(Three minutes later)

Phone: Ring — Ring — Ring.

Dad: I will have to go to Brookline after the office.

So it goes on like that until Dad leaves for the hospital. We don't see him until night. When he does come home, Sister, Mother and I climb all over him asking him questions about his day. But at supper it is like the morning — the phone is always ringing.

The only peaceful week end was when Dad went skiing up in New Hampshire. And even then there were five calls in three hours wondering where he was.

Sometimes Dad goes out on an emergency at 6 a.m. without any breakfast. We tell the patients that he will be home at 6 p.m., and he comes home at 11:15 p.m. Then he has a bowl of cold cereal and goes to bed. It might happen again tomorrow; we just can't depend on him.

On my birthday Dad was going to take my friends and me into Boston to celebrate. Fifteen minutes before going, the phone rang; Dad had an emergency and so we had to make different plans.

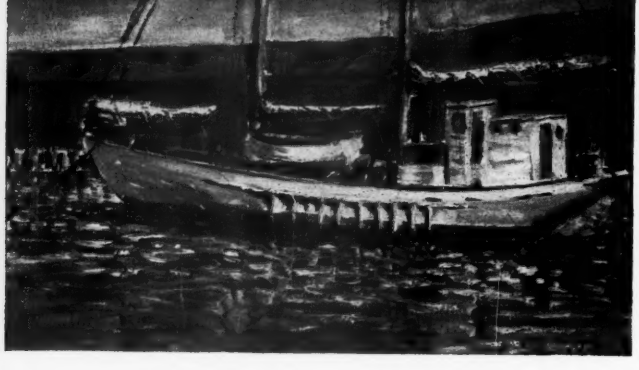
At this time, the phone was in the living room. At the table, Dad, Sister, Mother and I were eating breakfast.

Phone: Ring — Ring — Ring (I jumped up and ran at top speed to the phone).

Me: Hello. Yes, this is the doctor's home. Just a minute, please . . .

* * *

A year later. No more running. No more sprinting, because now we have a phone in the breakfast room!



Massachusetts Physicians Art Association

6. San Francisco Pilot Boat

(*Exhibited in Chicago, 1948*)

Oil Painting by

Arthur E. Spiller, M.D.

Ophthalmological Service

Boston City Hospital

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38291

PRESENTATION OF CASE

A seventy-two-year-old man was admitted to the hospital because of weakness.

The patient had been in reasonably good health until about a month prior to admission, when he first noted vague indigestion whose principal features were eructation and epigastric discomfort. His wife put him on a milk and cereal diet and he seemed to do well for a short time. Gradually, however, he became weaker and about two weeks prior to entry had to remain in bed because of this weakness, which gradually progressed until admission. His appetite had been poor, and he had eaten little; although he had complained of great thirst, he had taken very little fluid. He had had difficulty in passing urine, and for a short while before admission he had been incontinent of small amounts of urine. For the few days before admission he had been unable to speak, but he had apparently been aware of what was said to him.

There had been no fever, chills, cough, sputum, night sweats or chest or abdominal pain. His last bowel movement had been three days before admission.

Physical examination revealed an acutely ill, dehydrated, comatose man with a Kussmaul type of breathing. There was no characteristic odor to the breath. The mouth and throat were extremely dry, and the tongue thickly coated with a dry crust. The pupils were equal and reacted to light and accommodation. The neck veins were not dilated. The chest was emphysematous, and there was dullness to percussion with markedly decreased breath sounds in the right axilla and right base and some dullness and a few inspiratory rales at the left base. The heart rhythm was regular; the sounds were poorly heard but no murmurs were noted. The abdomen was flat. There was voluntary resistance to palpation in all quadrants of the abdomen, especially in the lower quadrants. A poorly defined, rounded mass was palpable in the left upper quadrant; no other palpable organs or masses were noted. There was some costovertebral-angle tenderness. Peristalsis was quiet and infrequent. Rectal examination revealed a non-nodular prostate diffusely enlarged to three times the normal size; bright-red blood was found in the stool. Neurologic examination was negative.

The temperature was 98°F., the pulse 104, and the respirations 32. The blood pressure was 80 systolic, 54 diastolic.

The urine had a pH of 5.5 and a specific gravity of 1.010 and gave a ++ reaction for albumin; the sediment was loaded with red cells and clumps of white cells. Examination of the blood showed a hemoglobin of 20 gm. and a white-cell count of 50,000, with 97 per cent neutrophils. The stools were reddish brown and gave a +++ guaiac reaction. The serum sodium was 149.9 milliequiv., the chloride 122 milliequiv., the potassium 5.8 milliequiv., and the carbon dioxide 11.5 milliequiv. per liter. The nonprotein nitrogen was 313 mg., and the total protein 4.40 gm. per 100 cc., with an albumin-globulin ratio of 0.7; the bilirubin was normal, and the cephalin-flocculation test was ++ in twenty-four and forty-eight hours. The prothrombin time was 23 seconds (normal, 13 seconds), and the pH of the blood 7.33. Roentgenograms of the chest showed clear lung fields, a prominent left ventricle and a moderately tortuous aorta. Films of the abdomen revealed a large, globular, soft-tissue mass in the left flank, measuring perhaps 20 cm. in length, occupying the region of the left kidney and extending down to the iliac crest; the left kidney could not be identified separately from the mass (Fig. 1). A gas bubble in the splenic flexure lay above and to the left of this mass. An electrocardiogram showed left-axis deviation. At catheterization 250 cc. of residual urine was found.

The patient was given 4000 cc. of fluid intravenously over the next twenty-four hours, and at the end of this time he was more alert. Physical examination was unchanged except that the tenderness and spasm were localized in the right lower quadrant; he protected his abdomen and begged not to be examined. The temperature was 102°F., the pulse 108, the respirations 50 to 60, and the blood pressure 100 systolic, 70 diastolic; the white-cell count was 26,300, the hemoglobin 15.5 gm., and the nonprotein nitrogen 367 mg. per 100 cc. He continued to be incontinent of feces, passing liquid, reddish-brown stools; the urinary output was negligible. He remained in a semicomatose state, with an elevated temperature and marked abdominal tenderness localized mostly to the right lower quadrant and no longer associated with definite spasm. The urinary output increased to 4000 cc. on the third day, when the nonprotein nitrogen was 280 mg. per 100 cc.; the urinary sediment contained 20 to 30 red cells and a few clumps of

white cells per high-power field. On the sixth hospital day he had massive bleeding from the rectum and required three transfusions. Physical examination showed a slight abdominal and right costovertebral-angle tenderness and the large mass in the left upper quadrant, which appeared to have a rather sharp edge near the mid-line; the abdomen was dull to percussion in this region but tympanitic from the costal margin up. The temperature was 100°F., the pulse 80, and the blood pressure 92 systolic, 40 diastolic; the hemoglobin was 9.5 gm. per 100 cc., the white-cell count 12,000, the bleeding

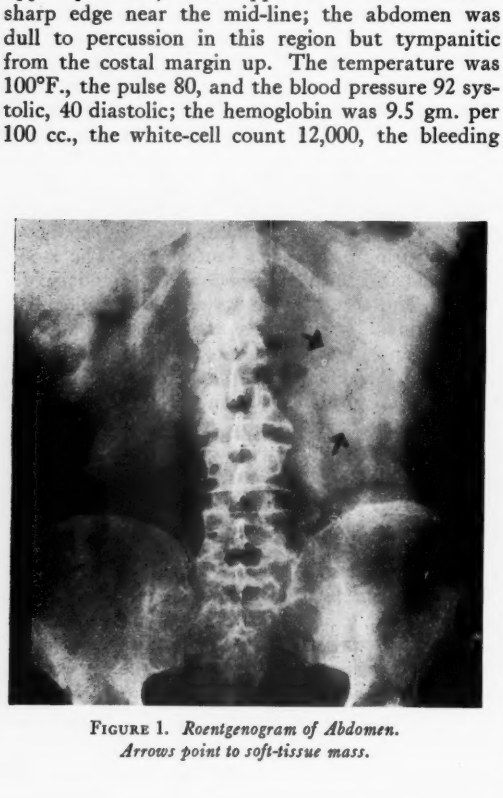


FIGURE 1. *Roentgenogram of Abdomen. Arrows point to soft-tissue mass.*

time 2½ minutes and the prothrombin time 18 seconds (normal, 13 seconds). The nonprotein nitrogen was 95 mg., the calcium 6.3 mg. and the phosphorus 2.9 mg. per 100 cc.; the carbon dioxide was 19.6 milliequiv., and the potassium 3.0 milliequiv. per liter. He continued to bleed massively from the rectum, and in spite of fifteen blood transfusions he developed progressive signs of shock and died on the tenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. MYLES P. BAKER*: The important findings on admission seem to me the story of anorexia and deepening stupor for two weeks prior to entry, the dehydration and acidotic breathing, somewhat more rapid than usually prevails in Kussmaul breathing, and the absence of fever. There was some suggestion in the physical examination of fluid in the right pleural cavity apparently not borne out by subsequent x-ray examination. The lower abdomen was definitely tender. The patient had an enlarged prostate, which did not suggest malignant disease when palpated. There was a freshly bloody stool in the rectum. There were no positive neurologic signs to account for the stupor. He had no hypertension.

The findings on laboratory examination were interesting. This dehydrated man could not concentrate urine, of which only one specific gravity determination, and that 1.010, was recorded; he had definite hematuria and some clumps of white cells in the urine, but infection in the urine was not a prominent feature. The fact that he was passing blood in the stools was confirmed on admission and became the prime clinical feature during the hospital stay. The serum electrolyte level seems to have been primarily due to dehydration in combination with renal insufficiency, as indicated by the extremely high level of the blood nonprotein nitrogen. The carbon dioxide level of 11.5 milliequiv. per liter seems to account for the type of breathing and tallies with the high nonprotein nitrogen level in confirming the suspicion of renal failure. The level of the blood nonprotein nitrogen seemed to me out of proportion to what one would expect in a dehydrated elderly person. There was no sure evidence of liver failure. The serum albumin was apparently reduced, as was the prothrombin concentration in the blood, but there was no other suggestion of liver failure. The prothrombin concentration seemed not sufficiently reduced to account in toto for the hemorrhage by rectum. He had a residual urine of 250 cc. — too small to indicate an obstructive uropathy as the chief cause of the renal insufficiency. Finally, the x-ray film confirmed the impression on physical examination of a left-upper-quadrant mass. The finding of a considerably larger mass than was made out by the examiner, I think, is very important and must have aroused many questions about its nature.

Would you show the x-ray films?

DR. JAMES J. MCCORT: A single posteroanterior chest film taken in bed demonstrates clear lungs and no fluid in the pleural cavity. Both lungs are moderately emphysematous. The heart is prominent in the region of the left ventricle, and the aorta is elongated and tortuous. On the abdominal film the most striking finding is an ill-defined soft-tissue mass in the left upper abdomen (Fig. 1). The stomach is displaced upward and to the right side, the gas-filled splenic flexure is displaced upward, and the descending colon is displaced laterally by the mass. The margin of the mass is quite smooth, and it contains no calcification. I believe it is separate from the spleen. It is not possible to identify either kidney or the psoas-muscle outline. A few flecks of calcium are seen in the prostate.

DR. BAKER: By the forcing of fluids intravenously, this patient became much better hy-

*Physician, Massachusetts General Hospital.

drated, as demonstrated by a more normal hemoglobin level for one thing. However, the blood nonprotein nitrogen level remained high. He continued to be incontinent of bloody stools and became for a while markedly tender over the entire abdomen and, I believe, particularly in the right lower quadrant. He began to run a fever and remained semiconscious. It is interesting that on the third day the urinary output became substantial; during the final week really massive hemorrhage from the rectum became the primary clinical feature, with a reduction of hemoglobin to 9.5 gm. There was no evidence of any blood platelet deficiency to account for the bleeding and no evidence of any blood dyscrasia. The blood nonprotein nitrogen level remained elevated though substantially lower than in the dehydrated state. The patient remained acidotic. There was noteworthy absence of hyperphosphatemia and hyperkalemia associated with the terminal uremic picture.

I believe this man had severe renal insufficiency in the presence of a large mass in the left side of the abdomen, which I think was consistent with a large polycystic kidney. The question comes up in that event, Why cannot we demonstrate an enlarged right kidney? It is certainly true that one may feel only one enlarged polycystic kidney although the other will be similarly involved in polycystic disease. Such a diagnosis would be more tenable were there bilateral tumors. Could this mass in the left flank have been any other sort of renal anomaly? I have read of so-called sigmoid kidney, but I should say this did not pass over far enough to the right side to be characteristic of such an anomaly. The insidious onset of uremia in this man is quite in keeping with the natural history of polycystic kidney. Such patients may lead an active and effective life right up to the last few weeks of terminal renal insufficiency, which develops unrelentingly at the end. The urinary sediment with hematuria and no mention of casts is just the sort of microscopical picture that one sees with the urine of polycystic kidneys.

Can these massive hemorrhages by rectum be explained on the basis of uremia? To be sure, although I have never seen a patient die of rectal hemorrhage in the presence of uremia, bleeding anywhere from the mouth to the anus in the gastrointestinal tract is a common manifestation in uremia. I should think that it would be entirely possible for such severe bleeding to be entirely caused by the so-called uremic colitis that the pathologist demonstrates for us. The fact that this man had a great deal of right-lower-quadrant abdominal tenderness is in keeping with such a premise because the necrotic lesions involving the lymphoid patches of the intestine are particularly common in the lower ileum, cecum and ascending colon.

To demand that, in addition to the renal insufficiency, this man had some sort of malignant lesion in the left side of the colon that would produce this massive bleeding seems to me unnecessary. I should expect, on the evidence that I have and my interpretation of it, that post-mortem examination would show a large cystic kidney on the left, a smaller cystic kidney on the right and the terminal picture of uremic necrotizing lesions in the colon, leading to hemorrhage.

Dr. B. J. Kennedy: Because of the mass in the left upper quadrant the service thought this patient had a carcinoma of the large bowel with perforation of the cecum as a complication, or pyelonephritis on the right or both. Because of the persistent bleeding the surgeons were urged to explore the patient; he was so weak that they refused.

Dr. Joseph C. Aub: I think Dr. Baker's still-life discussion was a great deal better than our moving-picture discussion of this patient. This man was so sick from the moment he came into the hospital that we did not do all the studies we should have liked to do. We did not feel the large mass in the left upper quadrant when he first came in. All the pain was in the left lower quadrant, and he had a great deal of spasm and some pulsation, as well as a white-cell count of 50,000. We were befuddled. When he improved markedly the mass in the left upper quadrant was palpable, and because it had large bowel above it, it could hardly have been spleen. I decided it was kidney too. We, however, were not content to make a diagnosis of uremia. My final opinion was that he had a hypernephroma that invaded the large bowel and produced hemorrhage from both the kidney and the large bowel. He just kept on bleeding as fast as we could put in blood.

Dr. William C. Quinby, Jr.: I saw this patient about twelve hours before he succumbed. I was unable to make any diagnosis at that time. The question was whether we should operate to stop the bleeding. Dr. F. B. Hershey, who had followed the patient with the Medical Service, and I both believed that at no time was he in sufficiently good shape to survive operation. I have nothing to add to the diagnostic picture concerning the nature of the abdominal masses because he was *in extremis* when I saw him, and examination of the abdomen was unreliable.

Dr. Aub: What puzzled me was the excessive bleeding. I wondered whether he did not have leukemia although there was no evidence for that diagnosis. His main symptom was that of bleeding, not of uremia.

Dr. Earle M. Chapman: I was wondering about myeloma; a myelomatous mass or leukemia could do that. I think this is a very difficult case.

Clinical Diagnoses

?Carcinoma of splenic flexure.

?Hypernephroma, with invasion of large bowel.

Benign prostatic hypertrophy.
Pyelonephritis.

Dr. Baker's Diagnoses

Polycystic kidneys.
Uremia.
Uremic colitis.

Anatomical Diagnoses

Necrotizing papillitis of kidneys.
Retroperitoneal cyst.
(Uremia.)
Gastrointestinal hemorrhage.
Benign prostatic hypertrophy, with obstruction.
Congenital kink of ureters.

Pathological Discussion

Dr. Benjamin Castleman: When the abdomen was opened, a very large cystic mass was found in the left flank. When the prosector cut through the mass, about a liter of clear, amber fluid gushed out. The cyst was unilocular, attached to the left leaf of the diaphragm, and extended down to the bifurcation of the aorta retroperitoneally. The kidney and adrenal gland were anterior to the cyst. The lining of the cyst was made up of connective tissue, not epithelial cells to suggest it came from a wolffian duct or was a dermoid; the best explanation is that it probably was a lymphatic type of cyst.

The immediate cause of death was found in the kidneys; each papilla of the kidneys was completely necrotic — a form of pyelonephritis, the so-called necrotizing papillitis. This type of renal disease is seen most often in diabetic persons, but in about a third of the cases it occurs in patients without diabetes; in these cases it is almost always associated with an obstruction of the urinary tract. This patient was not diabetic, but he had a very large prostate, trabeculation of the bladder and distended ureters on both sides. Another factor that aggravated the urinary obstruction was the presence of congenital kinks in both ureters about 10 cm. below the kidneys that produced some degree of obstruction because there was more dilatation above each kink than below. They were symmetrical, and I am sure they were congenital. Patients with necrotizing papillitis develop it very rapidly, have high white-cell counts, often have high fevers and usually die within a month.

We examined the entire gastrointestinal tract from the esophagus to the anus inch by inch and found no definite lesion except small petechial hemorrhages. The stomach contained 400 cc. of blood, and the entire colon and small bowel had blood, but when we washed away the intestinal contents, we found only the small mucosal hemorrhages. I do not see any other explanation for the bleeding than the uremia associated with the hemorrhages.

Dr. Aub: The bone marrow was normal?

Dr. Castleman: Yes.

Was he not a bit old for polycystic kidneys? My impression from our cases here is that these patients usually have hypertension and die between fifty and sixty years of age.

Dr. Baker: Addis[1] has a report of a series of 12 cases of polycystic kidneys in his book on glomerulonephritis; the average age was about fifty, but the blood pressure averaged only 150 systolic, 100 diastolic. The hypertension was not a marked feature. Dr. Young,[2] who included a collection of polycystic kidneys in his textbook, made the point that although most of them appear by the age of forty to sixty, some appear in the sixties and seventies.

Dr. Kennedy: Do you think we can explain the hemorrhage as being a result of the uremia?

Dr. Castleman: It is the only explanation we have for it. The liver was perfectly normal. There is no reason why it should have been caused by a prolonged prothrombin time.

Dr. Baker: In the cases of obstructing prostate, how often do you see necrotizing papillitis?

Dr. Fletcher H. Colby: In the last five years, we have had perhaps 3 or 4 cases, but we have never made the diagnosis beforehand.

Dr. Castleman: I think the obstructive element has been pretty well proved.[3] I recently heard of a patient at the Cushing Veterans Hospital who died of septicemia. He had a stone impacted at the lower end of one ureter, and at autopsy necrotizing papillitis was present only on the obstructed side.

Dr. Colby: It has occurred unilaterally in a few cases; the diagnosis has been made, and the patients have been operated on. I think there were 2 at the Boston City Hospital.

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CASE 38292

Presentation of Case

A sixty-six-year-old man entered the hospital because of shortness of breath.

Five months before entry the patient awoke from sleep extremely short of breath and mentally confused. He was hospitalized for three-and-a-half weeks at another hospital, where he was digitalized and discharged somewhat improved. He continued to take digitalis but was anorexic, weak and tired easily. Three months prior to entry edema of the ankles and swelling of the abdomen began to develop. Next he had an episode of pleuritic pain in the right lower portion of the chest, and fever and chills, followed by a hacking nonproductive cough. On admission to another hospital he was found to be confused and somewhat disoriented and to have a pleural effusion on the right, hepatomegaly and ankle edema. While in the hospital, he allegedly had some gastrointestinal bleeding. He

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improved somewhat after treatment with aureomycin, digitalis and a low-salt diet, but the mental confusion persisted and became progressively worse. He was discharged after six-and-a-half weeks but continued to have progressive dyspnea, orthopnea, weakness, easy fatigability and anorexia. The night before admission there was an increase in the dyspnea and orthopnea and increasing restlessness. There had not been any recent chest pain.

For the two years prior to entry he had a poor diet and had consumed large quantities of beer and wine. There had been no past illnesses of significance.

FIGURE 1.

Physical examination showed a moderately confused, dyspneic, orthopneic man with minimal cyanosis, distended neck veins and questionable scleral icterus. Respirations were Cheyne–Stokes in character. There was increased anteroposterior diameter of the chest. On the right, there was decreased tactile fremitus and vocal fremitus and decreased to absent breath sounds up to the level of the axilla, where there was egophony. Many medium moist inspiratory rales were heard at both bases, most marked on the right. The heart was enlarged with the point of maximum intensity at the left anterior axillary line; there was a forceful diffuse point of maximum impulse. The heart sounds were faint, a protodiastolic gallop was present at the apex, the heart rhythm was regular, and no murmurs were heard. A tender liver edge could be felt 5 fingerbreadths below the right costal margin. The spleen was not palpable. A smooth, firm, nontender prostate diffusely enlarged to twice the normal size was felt on rectal examination. There was no peripheral edema.

The temperature was 98.6°F., the pulse 110, and the respirations 40. The blood pressure was 120 systolic, 70 diastolic.

The urine gave a ++ reaction for albumin and a + reaction for sugar; the sediment contained 4 or 5 white cells and an occasional hyaline and granular cast per high-power field. Examination of the blood showed a hemoglobin of 13 gm. and a white-cell count of 13,700 with 84 per cent neutrophils; the platelets were reduced in number on examination of a blood smear. The nonprotein nitrogen was 27 mg., and the total protein 5.90 gm. with an albumin-globulin ratio of 1.4, and the bilirubin 0.7 mg. total per 100 cc.; the sodium was 132.7 milliequiv., the chloride 97 milliequiv., and the potassium 4.6 milliequiv. per liter. The prothrombin time was 16 seconds (normal, 13 seconds). The stools gave a + guaiac reaction. Thoracentesis on the right produced 800 cc. of straw-colored slightly cloudy fluid with a specific gravity of 1.014; the fluid contained 700 red cells and 35 white cells per cubic millimeter, of which 28 were neutrophils. Roentgenograms of the chest showed the heart to be considerably enlarged both to the left and posteriorly, predominantly in the region of the left ventricle. The lung fields were fairly hazy, and there was accentuation of the vascular markings. A large pleural effusion, which reached to about the fifth interspace in the axilla, was present on the right; there was considerable patchy density in the lung above the fluid level and an area of density at the right hilus (Fig. 1). An electrocardiogram showed left-bundle-branch block (Fig. 2).

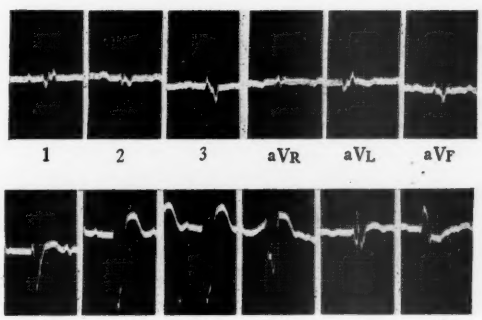

FIGURE 2.

The patient was given Cedilanid, aminophylline, digitoxin, Mercuhydrin and ammonium chloride. After the thoracentesis the dyspnea improved slightly, but the physical and mental state remained essentially the same; he was restless, disoriented and hallucinated. Terminally, he became oliguric, incontinent of urine and feces, and belligerent and combative. On the fourth day he suddenly took a long, gasping inspiration, became very cyanotic, began to twitch and died almost immediately.

Differential Diagnosis

Dr. Allan L. Friedlich*: I am faced with the problem of the sudden onset of dyspnea and confusion in a sixty-six-year-old man with a fairly rapid downhill course until his death five months later. In the absence of a history of any respiratory distress preceding the initial episode, this event immediately suggests pulmonary embolism or congestion secondary to left ventricular failure.

Later, abdominal swelling and ankle edema developed. In the light of subsequent physical findings this may be assumed to have been due to elevated venous pressure from embarrassment of the right side of the heart. Apparently, the edema was improved by the addition of a low-sodium regimen to the previous digitalis therapy because peripheral edema was not present on the final hospital admission. However, a progressive increase in dyspnea and orthopnea led to hospitalization again. Here the findings included cyanosis, neck-vein distention, rales in the lungs, right-sided pleural effusion, marked cardiac enlargement, with an apical protodiastolic gallop, and a large tender liver. These all support the hypothesis that the patient's major difficulty was due to congestive failure probably due to heart disease. However right-sided failure due to pulmonary disease may also have been a factor.

With this in mind, however, a review of the protocol reveals several features that are not so easily explained. Throughout the patient's illness mental confusion and disorientation were prominent features, and the cause is not obvious. Certainly, he was not uremic with a nonprotein nitrogen of 27 mg. per 100 cc. and only slight abnormality of the urine. I am told that he previously consumed large quantities of wine and beer and that the liver edge was palpated 5 fingerbreadths below the costal margin. The spleen was not palpable, the prothrombin time was only slightly prolonged, the total bilirubin was normal, and with the normal plasma proteins I doubt whether liver failure was an important factor. If the mental symptoms had appeared during treatment of congestive failure, one would suspect sodium depletion, but this was not the case and the blood sodium level was normal. Similarly, carbon dioxide retention seems unlikely as a cause of the mental aberrations. Cerebral emboli would have been likely to cause some localizing neurologic signs. I shall therefore have to ascribe the confusion and disorientation to congestive failure in a person with cerebral atherosclerosis.

The incident of pleurisy, chills, fever and dry cough that occurred a month or two before the patient entered this hospital may have been an unrelated pneumonia, but I would like to know whether or not he had real shaking chills and what the temperature was. In the absence of this information, pulmonary infarction is still a good possibility. I also do not know much about the gastrointestinal-tract bleeding observed at another hospital, but since the hemoglobin on admission here was 13 gm. per 100 cc. I doubt whether this was severe and it may have been related to the use of aureomycin.

The picture the patient presented was one of congestive failure with a larger liver than one would like to see and no fever, but a respectable elevation of the white-cell count to 13,700. These findings again make one think in terms of infarction. At this point perhaps we can get some help from Dr. Wyman. Would you show us the films, please?

Dr. Stanley M. Wyman: The enlargement of the heart is well seen and appears to affect chiefly the left ventricle. Fluid in both pleural spaces is demonstrated, the larger amount being in the right side of the chest. The right leaf of the diaphragm may be elevated. There is linear patchy density in the lower lung fields, especially on the right, and the hilar and pulmonary vascular shadows are diffusely increased in prominence. The right hilus contains a sharply defined rounded or ovoid shadow in the expected location of the interlobar artery. The bones are not remarkable.

Dr. Friedlich: Does that look like a carcinoma of the stomach extending into the stomach bubble?

Dr. Wyman: No; I should not dare draw that conclusion from these films, although I can by no means exclude the possibility.

Dr. Friedlich: Do you think that the configuration of the pulmonary artery on the right could represent thrombosis of the right pulmonary artery and if so, would this be likely to cause more dilatation of the main pulmonary-artery segment?

Dr. Wyman: I think that this possibility definitely exists and it had occurred to me independently; however, as you suggest, the main pulmonary artery and the arteries elsewhere do not appear particularly or unduly enlarged. I think with as much atelectasis as is present in the lower lobe, it is dangerous to draw such a conclusion from these films.

Dr. Friedlich: You can see no definite pulmonary infarct or scars of old infarcts?

Dr. Wyman: None that I can be completely sure of, although there are very suspicious densities in the right lower lobe that I have thought probably represent infarcts.

Dr. Friedlich: Evidence in favor of pulmonary infarcts, then, includes the sudden onset five months before admission, followed by edema, which subsequently cleared. There was an episode of pleurisy, pleural effusion, fever and now these suspicious x-ray findings.

If the protodiastolic gallop were on the basis of cor pulmonale alone one would expect it to be maximal not at the apex, but along the left sternal border. In addition, the electrocardiographic finding of left-bundle-branch block is further evidence of myocardial disease. In this age group coronary-artery disease is the most common cause of left-

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bundle-branch block. It is important to remember that this conduction defect alters the direction of depolarization of the ventricular septum so that early in the process of formation of the QRS complex the potential in the left ventricular cavity is positive, and hence important electrocardiographic evidence of myocardial infarction may be observed.

I wonder if I might see the electrocardiogram? As noted in the protocol, the pattern of left-bundle-branch block is present, and in addition there is prolongation of the PR interval. An unusual feature of the record is the presence of a negative deflection early in the QRS complex in Leads 1 and AVL. There is fairly marked elevation of the ST segments in Leads V_2 through V_6, and the R wave is smaller in Leads V_4 and V_5 than it is in Leads V_1 to V_3. It is hazardous to make an electrocardiographic diagnosis of myocardial infarction in the presence of left-bundle-branch block, but in this case I think the record is strongly suggestive.

I should like to explain earlier episodes as being due to pulmonary embolism and infarction, in a man with coronary-artery disease. This precipitated failure of the right ventricle. The most likely source of the emboli is the leg veins. In addition, shortly before entering this hospital it is probable that the patient had an anteroseptal myocardial infarction, which caused an increase in the already well marked failure of the left ventricle and led to his death.

Clinical Diagnoses

Pulmonary embolus.
Pulmonary-artery thrombosis, with infarction.
Hypertensive and arteriosclerotic heart disease, with failure.

Dr. Friedlich's Diagnoses

Multiple recurrent pulmonary infarctions.
?Thrombosis of right pulmonary artery.
Coronary-artery disease with congestive failure.
Anteroseptal myocardial infarction, probably recent.

Anatomical Diagnoses

Multiple pulmonary emboli, and infarcts, old and recent.
Phlebothrombosis, right calf.
Coronary sclerosis, severe with myocardial infarct, old.
Cardiac hypertrophy, left ventricle.
Pulmonary edema.
Hydrothorax, right.

Pathological Discussion

Dr. David Kahn: At autopsy we were able to corroborate quite well most of Dr. Friedlich's predictions. Although the pulmonary artery and its main branches were patent and unremarkable, scattered through the smaller pulmonary arteries, from the third division peripherally, there were multiple pulmonary emboli, varying from very recent ones that were not attached, to gray, granular ones that were firmly attached to the vessel walls. In the right lower lobe all the branches of the segmental arteries were plugged by emboli; the shadow noted on the x-ray film probably represented the lobar branch dilated proximal to this. In all the other lobes the distribution was more patchy and haphazard. There were multiple pulmonary infarcts scattered through all lobes; the right lower lobe contained the largest in number and the largest in size, one measuring up to 6 cm. in average diameter. Histologically, the infarcts were of different ages, varying from very recent hemorrhagic ones to very old ones consisting of linear scars, and the emboli likewise varied from very recent ones to some with partial to complete organization. Throughout all lobes there was marked pulmonary edema, and the right pleural cavity contained 1000 cc. of fluid.

The right popliteal vein and the veins of the right calf were thrombosed and were undoubtedly the source of these multiple emboli.

The heart was definitely enlarged, weighing 665 gm.; there was well marked hypertrophy of the left ventricle. The right ventricle measured 4 mm. in thickness, about the upper limits of normal. Both ventricles showed slight dilatation. There was marked coronary sclerosis, with severe narrowing, and as Dr. Friedlich predicted there was an anteroseptal myocardial infarct; however, this was an old rather than a recent infarct and histologically was compatible with a few months' duration — scar tissue that was still somewhat vascularized and contained a scattering of pigment-filled macrophages. Histologically, its age would be compatible with the episode causing his original hospitalization. There was no evidence of acute myocardial damage, and we suspect that the final episode was another pulmonary embolus; of course, acute myocardial insufficiency due to further decrease in the output of the left ventricle remains a possibility since he died much too quickly for anatomical changes to occur in the myocardium.

The cerebral vessels showed moderate sclerosis but no other lesions of significance on gross or microscopical examination. We have no better explanation than that already offered by Dr. Friedlich for the severe mental confusion. The liver and spleen were both markedly congested.

We have on a number of occasions discussed cases of recurrent pulmonary embolism at these exercises. Some of the patients lived for periods of two years or more, the case terminating finally with a clear-cut clinical picture of cor pulmonale. In the case discussed today, the course was too rapid for cor pulmonale to develop to any extent. Apparently, the recurrent emboli were enough to overburden an already barely compensated left ventricle, and terminally there was failure of both the right and left ventricles.

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INTERNATIONAL MEDICAL EXPERTS

AN expert, according to Webster, is "one instructed by experience; hence one who has special skill or knowledge in a particular . . . science or art." Too often, however, in the words of a recent editorial comment* "when one government seeks help from another" — and the implication is that it happens here as well as elsewhere — "the wrong experts are sent." These gentlemen defined in non-Websterian, but effective terms, as the "swivel-chair theorists" are hardly a credit to the country of origin and are unlikely to perform their tasks properly for the simple reason that they are not experts and they have not been instructed by experience. The country asking for help possesses plenty of educated physicians who can consult the textbooks and advance "conjectural reasoning." The need is for knowledge and experience.

The editorial rightly takes a jaundiced view of the occasional practice of dispatching a child to do a man's work simply because he holds the right titles in some organization or seems deserving of a junket with expenses paid. A pool of available experts is suggested — the elder statesmen of American Medicine, especially the group of men and women about to retire after fruitful, tested and truly expert service in practice, university or public life. "Many would welcome the opportunity to offer their services for a few weeks or months or even for several years if they could be assured of living and incidental expenses."

This plea for careful selection of visiting experts who truly have special skill and knowledge in their fields deserves support. In addition it is suggested that the visiting team — or some members of it, at least — would do well, not only to pay their respects to the "brass" but to reach into the grass roots of the country visited. For national leaders to visit national leaders is desirable and conventional. For prominent authorities to visit provincial areas, however, and confer directly with practicing physicians about every-day problems should result in accomplishments and dividends of good will that, while they may not make the biggest headlines, may perhaps contribute more than formal lectures and symposiums. Furthermore, just as in politics, the homely deed may engrave events more permanently in the minds of many than the flashy spectacle. Nehru is better remembered in New England for his visit to Wellesley College than for the formal call he paid on the White House.

A common difficulty in the function of experts is with the person who goes into a far country fully prepared to tell the inhabitants what to do, never having been out of the United States. Those whose whole idea of the universe is limited to their own part of a country are at a disadvantage exchanging information. "This is the way we do it in Boston" may be all right for Philadelphia but is not the correct application of knowledge to the problem of Lubbock, Texas — not to mention Delhi, India. One is reminded of the officer on Tinian who drafted a sign reading "Anyone who dumps garbage here is

*Editorial. Expert medical advice for foreign countries. *J. A. M. A.* 149:486, 1952.

subject to a fine of $300." The difficulty was that the natives of Tinian not only couldn't read "subject to a fine of" but didn't have $300 on the island.

The experts must be more than expert as defined by Webster; they must be broadly instructed by experience.

HAROFÉ HAIVRI

Harofé Haivri, the distinctively Hebrew medical journal of modern periodical literature, published semi-annually under the devoted editorship of Moses Einhorn, celebrates its silver jubilee with Volume 1 of 1952.

Established in New York in 1927 by a group of American Jewish physicians, *Harofé Haivri*, according to its current editorial by Dr. Einhorn, was to serve the purpose of "making a contribution to the science and art of healing in the Hebrew medium, and to make it in America, a land far removed from the center of the Hebrew revival."

A major difficulty, the editorial goes on to explain, has been the dearth of modern medical terminology in the Hebrew language — an apparent paradox when one considers the greatness of ancient Hebrew medicine and the significant contributions that have been made by Jews to modern medicine. These modern contributions, however, have been reported in the various current languages of the world, wherever Jews have settled and strengthened indigenous cultures with their own.

From the beginning a continuing effort has been made in a special section of the journal to deal with the problems of medical terminology and to develop a comprehensive vocabulary. This has perforce added weight to the Hebrew section of the journal and made it of increasing value. Of especial interest is the section on historical medicine, bringing old learning newly to light, for this ancient literature, as stated, is far from being exhausted as a field for research.

This quarter century of bringing and keeping up to date a culture that has added so notably to the sciences, Christian and Arabic as well as Hebrew, must be viewed with general respect.

"The task is great and laborious," writes the editor. "On this our Silver Jubilee we dare hope that, with the help of our old and faithful colleagues and with the cooperation of the writers and research workers in the field of Israeli medicine, the years before us will be even more fruitful and beneficent."

PAN AMERICAN SANITARY BUREAU

THE World Health Organization is pushing on with its plans to make the world a better place in which to live. In line with these efforts the Executive Committee of the Pan American Sanitary Organization recommended at its spring meeting a $2,060,000 budget for the 1953 health activities of the Pan American Sanitary Bureau, Regional Office of WHO for the Americas. This represents an increase of more than $100,000 over last year's allotment.

Various projects to improve the health of the Western Hemisphere are in preparation for the coming year. Environmental sanitation programs will be carried out in Nicaragua and Colombia, with consultative service extended to all member countries. Activities for the eradication of the *Aedes aegypti* mosquito, carrier of yellow fever, will be co-ordinated; further consultative and information services relating to the control of communicable diseases, public-health administration, public nursing, maternal and child health, nutrition, health education and medical care will be made available to the twenty-one American republics.

In greater detail, smallpox vaccination campaigns being launched this year in Ecuador and Bolivia will be continued into 1953, as will the vaccination campaign that was started in Peru in 1950; funds will be supplied for the Carlos Finlay Institute of Columbia and the Oswaldo Cruz Institute and National Yellow Fever Service of Brazil, which provide pathological, serologic and diagnostic services and yellow-fever vaccine to the other American countries. Fellowships will be provided for public-health training and assistance in venereal-disease control, and a program will commence next year for the eradication of Chagas disease in Uruguay.

And so the good-neighbor policy, out of which good neighborliness cannot but develop, continues.

GOPHERS AND PROGRESS

GOPHERS are coming into their own or at least a use has been discovered for these destructive inhabitants of the smooth golf fairway around the

Chicago area. Here, golfers have been mystified by the method of obtaining gophers: their burrows are filled with water, and they are trapped as they emerge.

Investigators at the University of Chicago are exploiting the ease with which these animals undergo hibernation when exposed to 40° temperatures over a forty-eight-hour period, to study this process as well as the response to lethal doses of x-rays in the dormant state. The state of hibernation depresses the metabolic rate in this animal, lowering the normal heart rate from 250 to 17 per minute.

All nonhibernating gophers exposed to 800 r died within fifteen days. Hibernating gophers, given the same dosage, but kept at 40° temperatures, remained alive for more than thirty days. Returning the gophers to normal activity two or four weeks after irradiation, resulted in typical symptoms of irradiation sickness, followed by death within fifteen days. The weight loss among nonhibernating, irradiated gophers was greater over the same period than that in the dormant animals.

From these data, a lowered metabolic rate seems a factor in protection against irradiation effects. Although drugs to decrease the metabolic rate will similarly protect against radiation effects, gophers present another method of study under natural conditions for this animal. Treatment of irradiation injury in the atomic age leaves much to be desired, and this work may add a clue to better therapy. A side effect, a reduction in gopher population, may be a boon to golfers.

To Correspondents. — *The following communications have been received: — Case of Incontinence of Urine; Case of Foreign Body in Knee Joint; Palmer's Artificial Leg; and Wonderful Pills.*

Boston M. & S. J., *July 21, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CORNWALL — Andrew P. Cornwall, M.D., of Boston, died on June 24. He was in his seventy-third year.

Dr. Cornwall received his degree from Tufts College Medical School in 1907.

He is survived by his widow, a son, a daughter, a brother and a sister.

GARLAND — Cornelius N. Garland, M.D., of Brookline, died on June 20. He was in his seventy-sixth year.

Dr. Garland received his degree from Leonard Medical School, Raleigh, North Carolina, in 1901. He was active in the organization of medical facilities for civilian defense in Brookline in World War II.

He is survived by a daughter.

HIRST — Elizabeth Hirst, M.D., of Melrose, died on June 9. She was in her sixty-second year.

Dr. Hirst received her degree from Boston University School of Medicine in 1913. She was school physician in Melrose.

Four sisters survive.

RICE — George A. Rice, M.D., of Holden, died on June 8. He was in his sixty-first year.

Dr. Rice received his degree from Tufts College Medical School in 1916. He was chief of staff of Holden District Hospital and a member of the staff of Holden Clinic, Rutland State Sanatorium, and was a fellow of the American Medical Association and American College of Chest Physicians and a member of the American Trudeau Society.

He is survived by his widow and two grandchildren.

STOKES — Leroy T. Stokes, M.D., of Haverhill, died on June 11. He was in his sixty-second year.

Dr. Stokes received his degree from Dartmouth Medical School in 1913. He was formerly medical examiner and a member of the School Board, Haverhill, and was chief of pediatrics at Hale and Benson hospitals, Haverhill. He was a fellow of the American Academy of Pediatrics and a member of the American Medical Association and the New England Pediatric Society.

He is survived by his widow, two sons, a daughter and a sister.

CORRESPONDENCE

DENTISTRY AND MEDICINE

To the Editor: In the June 26, 1952, number of the *New England Journal of Medicine*, your editorial, "The Forsyth Dental Infirmary for Children," should make it clear to all that dentistry is a medical specialty and that its study should be included in the medical curriculum. In the same issue of the *Journal*, your editorial, "Cui Bono," suggests the need of more dentists. It further suggests that a new dental school might be established. If new laws are to be made to ensure the creation of more dentists should not the law aim to give money to existing medical schools so that they can produce more graduates in that special field of medicine, at present known as dentistry?

CHANNING FROTHINGHAM, M.D.

Boston, Massachusetts

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Peptic Ulcer: Clinical aspects, diagnosis, management. Editor, David J. Sandweiss, M.D., associate attending physician, Division of Internal Medicine, Harper Hospital, Detroit. 8°, cloth, 790 pp., with 164 illustrations. Philadelphia: W. B. Saunders Company, 1951. $15.00. (Published under the auspices of the American Gastroenterological Association.)

This composite treatise on one of the most common diseases of the gastrointestinal tract is the work of 77 contributors. All the aspects of the disease are covered, including anatomy, physiology, pathogenesis, etiology, diagnosis and medical and surgical treatment. There is a special chapter on peptic ulcer in the young and aged. Lists of selected references are appended to the various chapters and there is a comprehensive index of 85 pages. The book is well published and is recommended for all medical libraries and to all physicians and surgeons interested in the subject.

Immuno-Catalysis: And related fields of bacteriology and biochemistry. By M. G. Sevag, Ph.D., associate professor, University of Pennsylvania School of Medicine. With a preface by Stuart Mudd, M.D., professor of bacteriology, University of Pennsylvania School of Medicine. Second edition, revised and enlarged. 8°, cloth, 547 pp., with 24 tables. Springfield, Illinois: Charles C Thomas, 1951. $12.00.

This new edition of a standard text, first published in 1945, has been enlarged and revised to bring the material up to date. Many new subjects of biochemical, enzymologic and immunologic interest have been added, including a chapter on the physiology and biochemistry of anaphylaxis. The printing has been done with a good legible type, on soft paper. There is an extensive bibliography and indexes of authors and subjects. The book should be in all collections on bacteriology, immunology and biochemistry.

Die neuzeitlichen Brustwand- und Extremitäten-Ableitungen in der Praxis. By Prof. Dr. Herbert Reindell, Oberarzt der medizinischen Universitätsklinik Freiburg i. Br., and Dr. Helmuth Klepzig, Assitent der medizinischen Universitätsklinik Freiburg. With a foreword by Prof. Dr. Ludwig Heilmeyer, Direktor der medizinischen Universitätsklinik Freiburg. 8°, cloth, 179 pp., with 64 illustrations. Stuttgart: Georg Thieme, 1951. Ganzleinen DM 22.50. Distributed by Grune & Stratton, Inc., New York City.

This monograph covers the literature on electrocardiography. The chapters discuss the various methods, the normal EKG and the diagnosis of infarcts and diseases of the heart. There are indexes of authors and subjects and a bibliography of 10 pages. The publishing is excellent; the electrocardiograms are especially good. The book should be in all collections on the subject.

Rosenau Preventive Medicine and Hygiene. By Kenneth F. Maxcy, M.D., Dr.P.H., professor of epidemiology, Johns Hopkins University School of Hygiene and Public Health. Seventh edition. 8°, cloth, 1462 pp., with 49 illustrations. New York: Appleton-Century-Crofts, Incorporated, 1951. $14.00.

The standard work of the late Dr. Rosenau has been continued by Dr. Maxcy as a collective book by 26 collaborators, all authorities in their special fields. Each of the fifty subjects is documented with a list of references. There is a good index, and the publishing is excellent. The book is recommended for all medical libraries and public-health organizations.

The Pathogenesis of Tuberculosis. By Arnold R. Rich, M.D., Baxley Professor of Pathology, Johns Hopkins University School of Medicine, and pathologist-in-chief, Johns Hopkins Hospital, Baltimore, 1951. Second edition. 8°, cloth, 1028 pp., with 89 illustrations and 20 tables. $15.00.

This second edition of a standard work on tuberculosis has been entirely revised and new material added to bring the subject up to date. A comprehensive review of the pertinent literature is incorporated in the text. There is a bibliography of 1500 references. There are indexes of authors and subjects, and the publishing is excellent. The book should be in all collections on the subject.

Surgical Care: A practical physiologic guide. By Robert Elman, M.D., professor of clinical surgery, Washington University School of Medicine, assistant surgeon, Barnes Hospital, associate surgeon, St. Louis Children's Hospital, and director of surgical service, H. G. Phillips Hospital, St. Louis. 8°, cloth. 586 pp., with illustrations. New York: Appleton-Century-Crofts, Incorporated, 1951. $8.00.

Dr. Elman, in this book on surgical care, has had the help of twenty-seven specialists, who have either contributed material or read the chapters in their special fields. The relevant literature is reviewed throughout the various chapters, and there are indexes of authors and subjects. The publishing is excellent.

The Normal Cerebral Angiogram. By Arthur Ecker, M.D., Ph.D. (Neurology), surgical neurologist, Syracuse, New York. 8°, cloth, 190 pp., with 140 illustrations. Springfield, Illinois: Charles C Thomas, 1951. $6.50.

This text of this special monograph is divided into two parts, on technic and on angiographic anatomy. The anatomic part is essentially an atlas. The illustrations are excellent. The small book should be in all collections on neurology.

Patterns of Disease: On a basis of physiologic pathology. By Frank L. Apperly, M.A., M.D. (Oxford), D.Sc. (Melbourne), F.R.C.P. (London), professor of pathology, Medical College of Virginia. 8°, cloth, 456 pp., with 50 illustrations and 37 charts. Philadelphia: J. B. Lippincott Company, 1951. $8.00.

The text of this new book on physiologic pathology is based on lectures given at the Medical College of Virginia. The material is generally arranged according to the systems of the body. The final chapter briefly discusses diseases resulting from psychic disturbances and psychic disturbances following disease. There is a good index and the publishing is well done.

Therapy of Dermatologic Disorders, including a Guide to Diagnosis and a Dermatologic Pharmacopeia. By Samuel M. Peck, M.D., dermatologist, Mount Sinai Hospital, New York City, associate clinical professor of dermatology, Columbia University, New York City, and medical director (R) inactive, U.S.P.H.S.; and George Klein, M.D., associate visiting dermatologist, Morrisania City Hospital, New York City. acting adjunct, Mount Sinai Hospital, and assistant clinical professor of dermatology, New York Medical College. 8°, cloth, 384 pp., with 4 illustrations. Philadelphia: Lea & Febiger, 1951. $6.50.

This new book is written for the practicing dermatologist and is principally devoted to therapeutics. There are special chapters on physical therapy and venereal diseases. Part Three is a dermatologic pharmacopeia, listing in alphabetical order the agents used in the treatment of diseases of the skin. There is a valuable appendix on the removal of medicinal stains. There is a good index, and the book is well published.

A Course in Practical Therapeutics. By Martin E. Rehfuss, M.D., professor of clinical medicine, and Sutherland M. Prevost, lecturer in therapeutics, Jefferson Medical College, Philadelphia, and attending physician, Jefferson Medical College Hospital, and Alison H. Price, M.D., associate professor of medicine, Jefferson Medical College, assistant physician, Jefferson Medical College Hospital, and chief of diabetic clinic, Curtis Clinic. Second edition. 4°, cloth, 938 pp., with 96 plates. Baltimore: The Williams and Wilkins Company, 1951. $15.00.

This standard book on therapeutics was first published in 1948 and has been reprinted twice. The work is the joint effort of seventeen contributors. This new edition has been revised to bring it up to date. There is a comprehensive index, and a good type face has been used. The publishing is well done.

Diseases of the Ear, Nose, and Throat: A textbook of clinical and laboratory procedures. By Georges Portmann, M.D., professor of oto-rhino-laryngology, University of Bordeaux, dean of the School of Medicine and Pharmacy, University of Bordeaux, surgeon, Hospital of Tondu, Bordeaux, and surgeon, Hospital Leopold Bellan, Paris. Translated by Fernand Montreuil, M.D., and Jules G. Waltner, M.D. 4°, cloth, 728 pp., with 645 illustrations and 11 plates. Baltimore: The Williams and Wilkins Company, 1951. $20.00.

This English translation of the textbook of the eminent French otolaryngologist is a credit to its publishers. The illustrations are excellent, and there is a good index. The book should be in all collections on the subject.

The Psychoanalytic Study of the Child. Volume VI. 8°, cloth, 398 pp. New York: International Universities Press, Inc., 1951. $7.50.

This volume of a standard series contains the papers read at a two-day discussion meeting, April 23-24, 1950, held at the Austen Riggs Foundation, Stockbridge, Massachusetts. Seventeen specialists, including Anna Freud, took part in the discussions. The material is divided into five categories: problems of child development, masturbation, early childhood, latency and adolescence. A table of the contents of the previous volumes is appended to the text. The lack of an index detracts from the reference value of the volume. The series should be in all collections on psychoanalysis.

The 1951 Year Book of Drug Therapy (September 1950–August 1951). Edited by Harry Beckman, M.D., director, Department of Pharmacology, Marquette University Schools of Medicine and Dentistry, and consulting physician, Milwaukee County General and Columbia Hospitals. 12°, cloth, 502 pp., with 91 illustrations. Chicago: The Year Book Publishers, Inc., 1951. $5.00.

This yearbook comprises part of the series of *Practical Medicine Year Books* and surveys the literature for a complete year in its field. The abstracts are arranged alphabetically by subject and are of sufficient length to give a good summary of the article noted. There are indexes of authors and subjects and the small book is well published. It should be in all medical reference collections.

The 1951 Year Book of Radiology (June, 1950–June, 1951). Radiologic Diagnosis. Edited by Fred J. Hodges, M.D., professor and chairman, Department of Roentgenology, University of Michigan, and John F. Holt, M.D., associate professor of roentgenology, University of Michigan. *Radiation Therapy.* Edited by Harold W. Jacox, M.D., professor of radiology, Columbia University College of Physicians and Surgeons, chief, Radiation Therapy Division, Radiologic Service, Presbyterian Hospital, New York City, and Vincent P. Collins, M.D., associate professor of radiology, Columbia University College of Physicians and Surgeons, director, Department of Radiation Therapy, Francis Delafield Hospital, and attending radiologist, Presbyterian Hospital. 8°, cloth, 394 pp., with 368 illustrations. Chicago: The Year Book Publishers, Inc., 1951. $7.00.

The text of this year book is divided into two parts, on radiologic diagnosis and on radiation therapy, which today form almost two special fields in medicine. There is a good index. The set should be in all medical reference collections and could prove valuable to radiologists of both classes.

Syphilis. By Richard S. Weiss, M.D., dermatologist-in-chief, Barnard Free Skin and Cancer Hospital, St. Louis, and Herbert L. Joseph, M.D., consultant in dermatology and syphilology, United States Air Force Base and Travis Air Force Base, California, and instructor, Department of Medicine, Division of Dermatology, Stanford University School of Medicine. 8°, cloth, 180 pp., with 42 illustrations. New York: Thomas Nelson and Sons, 1951. $3.00.

This manual is written especially for physicians who usually see syphilis cases first. It stresses the need of supplementary treatment, in addition to penicillin, and the need of follow-up studies. The chapters are relatively short and concise.

Clinical Allergy: A practical guide to diagnosis and treatment. By Samuel J. Taub, M.D., professor of medicine and chairman, Department of Allergic Diseases, the Chicago Medical School, professor of medicine, Cook County Graduate School, and attending physician, Cook County, Columbus and Mt. Sinai Hospitals. Second edition. 8°, cloth, 276 pp. New York: Paul B. Hoeber, Incorporated. 1951. $4.50.

The first edition of this book was published in 1945. The author has revised his text to bring it up to date. The thermostable antibody, reverse passive transfer and inverse anaphylaxis are described and their clinical significance in practice pointed out. The antihistaminic drugs, with their dosages and indications, and the use of ACTH and cortisone, especially in chronic intractable asthma, are included in the new material.

Histologie und mikroskopische Anatomie des Menschen. Erster Band, Zellen-und Gewebelehre. Zweiter Band, Organe und Systeme. By Dr. Wolfgang Bargmann, o.ö. Professor d Anatomie an der Universität Kiel. 4°, cloth. Vol. 1, 2 pp., with 193 illustrations. Vol. 2, 563 pp., with 412 illu trations. Stuttgart: Georg Thieme, 1951. Vol. 1, geb. DM 19.60. Vol. 2, geb. DM 45.00. Distributed by Grune a Stratton, Incorporated, New York.

This two-volume set on histology and microscopical anatomy is well written and excellently published. In Volume One are discussed the cell and tissue. Volume Two is devoted to the special systems and organs of the body. Lists of references are appended to the various chapters, and indexes conclude each volume. The illustrations are excellent. The set should be in all collections on histology.

Industry and Tropical Health. Proceedings of the First Industrial Tropical Health Conference, sponsored by the Harvard School of Public Health, December 8-10, 1950, at Boston, Massachusetts. 4°, cloth, 314 pp., with illustrations. New York: Robert W. Kelly Publishing Corporation, 1951. $10.00.

This volume presents in short form the various papers read at the twelve sessions of the conference. The first to fourth meetings were devoted to industry and health in the Middle East, tropical Africa, the Far East and tropical America. The other sessions were concerned with the organization of industrial health services, the use of antibiotics in certain tropical diseases, nutrition, the current research program of the Harvard School of Public Health, infectious diseases and problems of control and health hazards in industry. The book is well illustrated. An appendix provides short biographical sketches of the industrial delegates. There is a good index and the publishing is excellent. The book should be in all collections on public health and on industrial and tropical medicine.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

JULY 24–26. Conference on Aging. Page 559, issue of April 3.

AUGUST 25–29. American Congress of Physical Medicine. Page 476, issue of March 20.

AUGUST 31–SEPTEMBER 6. Interamerican Congress of Cardiology. Page 522, issue of March 27.

SEPTEMBER 7–9. Combined session of the New Hampshire and Vermont State Medical Societies. Mount Washington Hotel, Bretton Woods, New Hampshire.

SEPTEMBER 8–20. First Argentine Congress of Thoracic Surgery. Page 1024, issue of June 26.

SEPTEMBER 24. Massachusetts Academy of General Practice. Fall meeting. Hotel Statler, Boston.

OCTOBER 28–30. New England Postgraduate Assembly. Hotel Statler, Boston.

OCTOBER 29. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

NOVEMBER 2–7 AND 10–21. Courses in Laboratory Diagnosis of Tuberculosis. Page 354, issue of February 28.

NOVEMBER 9 AND 10. American Society for the Study of Arteriosclerosis. Page 78, issue of July 10.

DECEMBER 7. American Academy of Dental Medicine. Hotel Statler, New York City.

JULY, 1953. International Congress on Medical Librarianship. Page 316, issue of February 21.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 24

THURSDAY, JULY 24

*8:30–10:00 a.m. Fracture Conference. Boston City Hospital.
*9:00–10:00 a.m. Grand Rounds. House of the Good Samaritan.
*9:00–10:00 a.m. Cardiac Grand Rounds. House of the Good Samaritan.
*9:00–10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
*4:00–5:00 p.m. Medical Division Lecture. Mount Auburn Hospital, Cambridge.

FRIDAY, JULY 25

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Pediatrics. Woolson II, Mount Auburn Hospital, Cambridge.

(*Notices concluded on page xvii*)